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SURGERY

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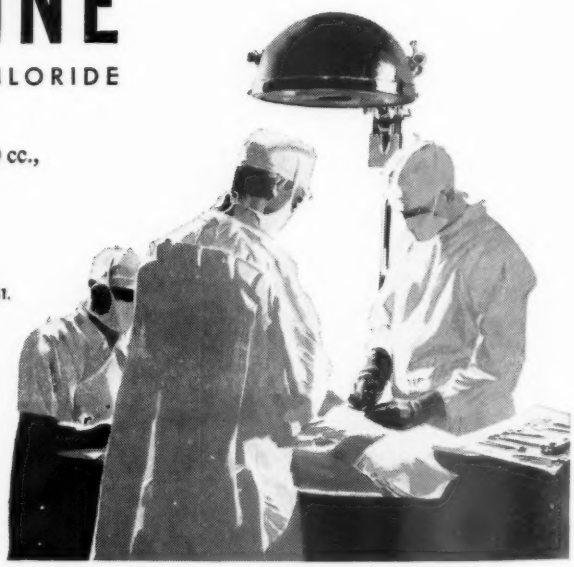

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SURGERY

VOL. 41 FEBRUARY, 1957 No. 2

Announcement

REAPPRAISAL SECTION

SURGERY announces the institution of a Reappraisal section.

Many authors who contribute to SURGERY and other surgical journals limit their publications to a small number of sound papers, widely spaced in time. Others describe concepts still in the process of development. In the belief that readers are at a loss to know the current stands of many authors and will welcome from them fresher statements relating to their present positions concerning the problems at hand, the Editors are adding a new section to SURGERY (see page 342 of this issue). This Reappraisal section should serve the special purpose of acquainting our readers with an author's current views upon a subject concerning which he has earlier expressed himself. Such reappraisals may pertain to techniques, physiologic implications, therapeutic approaches, or considerations of pathologic physiology.

The Editors of Reappraisal will select from the surgical literature papers or concepts which seem to come into this category of interest. Specific questions will be asked of selected authors. Initially, attention will be concentrated on papers that have appeared in surgical journals, largely American, within recent years. We will be pleased to include in Reappraisal contributions which seem appropriate for publication in this section.

It is believed that the opportunity to reorient readers concerning any changes in points of view will be welcomed by authors, especially since these reconsiderations can usually be documented very briefly. We hope that, in the near future, former authors who have found reason to revise previously published conclusions will contribute spontaneously their present concepts to the Reappraisal section. These contributions will be welcomed and will be published if the Editors judge them to hold pertinent meaning to surgeons.

It is our hope that contributions to this section will prove helpful in providing the profession throughout the broad field of surgery with an understanding of the present views of leaders in the various aspects of that field.

CLARENCE DENNIS
ALFRED HURWITZ

Original Communications

Society for Vascular Surgery
(Concluded)

THE EFFECT OF GENERALIZED VASODILATATION UPON THE SYMPATHECTOMIZED EXTREMITY

THOMAS O. MURPHY, M.D., JOHN J. HAGLIN, M.D.,* AND DAVITT A. FELDER, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School and Minneapolis General Hospital, Minneapolis, Minn., and St. Joseph's Hospital, St. Paul, Minn.)

GENERALIZED vasodilatation induced by body heating or chemical agents has been a useful diagnostic and therapeutic procedure in peripheral vascular diseases.[6, 8, 9] There are many reports in the literature about the effectiveness of chemical vasodilators as noted in the extensive review on this subject by Nickerson.[10] These agents have enjoyed great popularity. Under certain conditions, however, effecting a generalized vasodilatation may be physiologically ill advised.

DeBakey, Burch, Ray, and Ochsner[5] noticed that following lumbar sympathetic nerve block the digital pulse volume and skin temperatures increased on the blocked side while in the opposite extremity there was a decrease in digital pulse volume and skin temperature. From this evidence they proposed a "borrowing-lending" (hemometakinesia) blood volume relationship between the sympathetically denervated extremity and the rest of the body.

In five patients Buchanan, Cranley, and Linton[2] reported a decrease in digital pulse volume in the sympathectomized extremity with body heating. They concluded that this decrease was a result of generalized vasodilatation and in keeping with the "borrowing-lending" phenomenon or "hemometakinesia" of DeBakey and his co-workers.[5]

Van Itallie and Clarke,[11] in a study of three sympathectomized extremities using venous occlusion and peripheral pulse volume techniques, reported a decrease in digital blood flow after body heating even though there was only a minimal decrease in pulse volume. With Priscoline after heating they noticed a slight decrease from the initial postsympathectomy blood flow.

Read at the tenth annual meeting of the Society for Vascular Surgery, Chicago, Ill., June 10, 1956.

*Lewis and Maude Hill Family Foundation Research Fellow.

This is a report of our observations on the effect of generalized vasodilatation, mainly on digital pulse volume, before and after lumbar sympathectomy.

METHOD

Patients with occlusive arterial disease of the lower extremities were studied in a controlled temperature room at 20° C. and 35° C. in the supine position. The patient was in a fasting state, covered with a hospital gown, and was allowed to equilibrate between studies until skin temperatures were constant. The postsympathectomy studies were done from two months to two years after operation, except for two cases which were five years after operation.

The digital pulse volume was studied with a Grass Electroplethysmograph* after the method of Cranley, Buchanan, Simeone, and Linton.[3] Skin temperatures of both first and fifth toes and both index fingers and room temperatures were periodically recorded in close succession with an eight-lead Brown Electronic apparatus.† The controlled-temperature room was held within 1.5° C. of the set point.

Forty-five extremities were studied before sympathectomy to evaluate the response of the digital pulse volume of the toe to whole-body heating.

Eighty-six extremities were studied after lumbar sympathectomy to evaluate the response of the sympathectomized digit in the cold room at 20° C. and to whole-body heating at 35° C.

The effect of Priscoline‡ (2-benzyl-4, 5-imidazoline hydrochloride) was studied on a group of 24 sympathectomized extremities at 20° C. Fifty milligrams of Priscoline was given intravenously, and skin temperatures and the digital pulse volume of the sympathectomized digit were recorded. In six extremities of this group the effect of Priscoline on the digital pulse volume of the unsympathectomized index finger was studied simultaneously.

All of the above patients ranged in age from 44 to 70 years.

Following the injection of Priscoline the blood pressure and pulse rate were recorded at three-minute intervals. The pulse volume and skin temperature values used in the determination of results were those after the blood pressure and pulse rate had returned to the preinjection levels.

A separate group of 44 unsympathectomized extremities in 22 patients over 70 years of age was studied in the controlled-temperature room in the manner previously described. The ages ranged from 70 to 91 years.

RESULTS

All of these extremities clinically fall into the advanced arteriosclerotic groups II-IV as defined by Cranley's[4] classification. Still the degree of obliterating disease is difficult to classify accurately. For this reason we have chosen to compare the results of each extremity with itself rather than to some standard.

*Grass Instrument Company, Quincy, Mass.

†Brown Instrument Co., Division of Minneapolis Honeywell Regulator Co., Philadelphia, Pa.

‡Ciba Pharmaceutical Products, Inc., Summit, N. J.

I. *Presympathectomy—45 Extremities.*—Table I shows the relative change of the digital pulse volume in the second toe in the presympathectomy group. Six of the extremities showed a slight decrease or no change in the pulse volume with heat vasodilatation. Eleven extremities had an increase up to 100 per cent. Twenty-eight extremities showed an increase of over 100 per cent in the digital pulse volume and three of these extremities had over a tenfold increase.

TABLE I. RELATIVE CHANGE IN DIGITAL PULSE VOLUME WITH WHOLE-BODY HEATING BEFORE SYMPATHECTOMY
(45 Studies)

PER CENT CHANGE	NUMBER
Slight decrease or no change	6
Per cent increase	
0-100	11
100-200	7
200-300	4
300-400	3
400-500	3
500-600	3
600-700	2
700-900	2
900-1,000	1
Over 1,000	3

2. *Post Sympathectomy—45 Extremities.*—Table II shows the relative change in digital pulse volume in the second toe with sympathectomy, at 20° C. Two extremities had a decrease in pulse volume of less than 10 per cent. Five extremities showed a 0 to 100 per cent increase in pulse volume. Thirty-eight extremities had an increase of more than 100 per cent and 17 of these extremities showed over a tenfold increase in pulse volume.

TABLE II. RELATIVE CHANGE IN DIGITAL PULSE VOLUME WITH SYMPATHECTOMY, AT 20° C.
(45 Studies)

PER CENT CHANGE	NUMBER
Slight decrease	2
Per cent increase	
0-100	5
100-200	3
200-300	3
300-400	4
400-500	1
500-600	6
600-700	1
700-900	1
900-1,000	2
Over 1,000	17

3. *Post Sympathectomy With Whole-Body Heating—86 Extremities.*—In this group (Table III) 7 extremities had an increase in pulse volume. Eight extremities showed little change in the sympathectomized limb. In 51 extremities a drop in pulse volume of 5 per cent to 40 per cent was noted and in 20 extremities the fall was from 40 per cent to 85 per cent of the original pulse volume in the cold room.

TABLE III. RELATIVE CHANGE IN DIGITAL PULSE VOLUME WITH WHOLE-BODY HEATING AFTER SYMPATHECTOMY
(86 Studies)

PER CENT CHANGE	NUMBER
1-100 Increase	7
0-5 Decrease	8
5-10 Decrease	7
10-20 Decrease	19
20-30 Decrease	11
30-40 Decrease	14
40-50 Decrease	10
50-60 Decrease	9
60-85 Decrease	1

4. *Post Sympathectomy-Priscoline Studies—24 Extremities.*—Table IV shows the changes in the digital pulse volume of the second toe of the sympathectomized limb after the administration of Priscoline intravenously. Two extremities had an increase in pulse volume, both of which were less than 20 per cent. Eight extremities had a 0 to 25 per cent decrease and the remaining 14 patients had a 25 to 84 per cent decrease in pulse volume.

TABLE IV. RELATIVE CHANGE IN DIGITAL PULSE VOLUME WITH INTRAVENOUS PRISCOLINE AFTER SYMPATHECTOMY, AT 20° C.
(24 Studies)

PER CENT CHANGE	NUMBER
Increase	2
Per cent decrease	
0-25	8
25-50	8
50-75	2
75-84	4

In Table V comparison of the relative changes in the digital pulse volume in the unsympathectomized index finger and the sympathectomized second toe recorded simultaneously after intravenous Priscoline demonstrates that the pulse volume in the toe decreased or showed no change, while that in the finger increased in 5 out of these 6 patients. The temperature of the first and fifth toes of the sympathectomized limbs did not change. However, the temperature of the unsympathectomized index finger increased an average of 2° C.

TABLE V. COMPARISON OF THE RELATIVE CHANGES IN THE DIGITAL PULSE VOLUMES OF THE FINGER AND THE SYMPATHECTOMIZED TOE WITH INTRAVENOUS PRISCOLINE, AT 20° C.

PATIENT	FINGER (PER CENT)	TOE (PER CENT)
J. L.	+ 50	–40
E. C.	No change	–50
G. J.	+ 65	No change
E. G.	+ 50	–56
G. K.	+640	No change
P. G.	+410	– 8

5. *Whole-Body Heating in Unsympathectomized Extremities Over Age 70—44 Extremities.*—Table VI shows that in a group over 70 years of age 25 extremities had an increase in pulse volume in the second toe while 19 extremities had a decrease in the pulse volume with whole-body heating.

DISCUSSION

In the presympathectomized limb the relative increase in digital pulse volume with whole-body heating may be great even in the arteriosclerotic extremity (Table I). Repeated studies in this same group show that with sympathectomy the relative increase in pulse volume is greater than that effected by whole body heating preoperatively (Table II). However, generalized vasodilatation induced by either whole-body heating (Table III) or Priscoline (Table IV and V) results in a decrease in digital pulse volume in the sympathectomized extremity.

In all of these instances there seems to be a redistribution of blood volume as well as changes in flow rate. In the group with preoperative body heating, blood is shifted from the viscera and muscle to the periphery as a physiologic heat-regulating mechanism.[1] In the next series of studies after sympathectomy, there is an increase in blood flow to these limbs as documented by the studies of Herrick, Essex and Baldes,[7] while the rest of the periphery is still vasoconstricted due to cold. When the body is subjected to generalized vasodilatation due to whole-body heating or Priscoline, we believe that the sympathectomized limb with its relatively fixed blood volume and peripheral resistance is affected by changes of blood volume and resistance elsewhere, resulting in a redistribution of flow to the detriment of the sympathectomized extremity. This explanation is suggested by the experiment of DeBakey,[5] and is in keeping with the "borrowing-lending" phenomenon.

TABLE VI. RELATIVE CHANGE IN DIGITAL PULSE VOLUME WITH WHOLE-BODY HEATING IN PATIENTS OVER 70 YEARS OF AGE
(44 Studies)

PER CENT CHANGE		NUMBER
Over 100	Increase	19
50-100	Increase	4
0-50	Increase	2
0-50	Decrease	18
50-57	Decrease	1

In the unsympathectomized normal and arteriosclerotic extremity there is a reasonably high correlation between pulse volume and blood flow as shown by Winsor.[12] Assuming the validity of this correlation and the reasonable theory of hemometakinesia, the increase in pulse volume and skin temperature in the relatively normal index finger allows us to assume that the simultaneous decrease in pulse volume of the sympathectomized limb probably represents a diminution in blood flow.

The apparent discrepancy between our findings and those of Van Itallie and Clarke[11] can probably be explained by the fact that our studies were made: (1) on a larger number of extremities; and (2) under controlled environmental temperature conditions and the Priscoline studies were done in a cold environment.

On examining the laboratory results of whole-body heating on the digital pulse volume in a large group of unsympathectomized arteriosclerotic extremities,

it was noticed that above the age of 70 a high percentage of the patients (Table VI) showed a drop in pulse volume with whole-body heating. These patients have an increased peripheral resistance and decreased neurovasomotor activity and the shifting of blood may be detrimental to a high number (43 per cent) of such extremities even though unsympathectomized.

SUMMARY AND CONCLUSIONS

The effect of generalized vasodilatation on intact and the sympathectomized arteriosclerotic extremities has been studied under controlled environmental conditions. These studies have shown a consistent decrease in the plethysmographic pulse volume in the sympathectomized limb after chemically and thermally induced generalized vasodilatation. Based on the results of these findings we believe that generalized vasodilatation may be detrimental to the ischemic sympathectomized extremity.

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EVALUATION OF THE TRANSMETATARSAL AMPUTATION IN PATIENTS WITH DIABETES MELLITUS

FRANK C. WHEELOCK, JR., M.D.,* JOHN B. MCKITTRICK, M.D.,** AND HOWARD F. ROOT, M.D.,*** BOSTON, MASS.

(From New England Deaconess Hospital)

McKITTRICK and co-workers[2] in 1949 reported their experiences with the use of the transmetatarsal amputation in diabetic patients having lesions of the feet due to neuropathy or infection (with good circulation) or due to arterial insufficiency. Since then we have continued to utilize this procedure at the New England Deaconess Hospital with the conviction that it obviated many higher amputations and produced a useful foot. As the problems of its use have been discussed with colleagues throughout the country, we have learned that the results have been discouraging to many surgeons. It therefore seemed to us that a re-evaluation of our results and methods was needed. All the patients studied had diabetes mellitus and most of them were referred by the Joslin Clinic. The immediate and long-term results were evaluated and correlated with the indication for operation and the condition of the circulation at the time of operation. We wish to thank Drs. T. C. Pratt and C. C. Franseen for permission to include their patients.

SELECTION OF PATIENTS FOR TRANSMETATARSAL AMPUTATIONS

There are two clear-cut groups of diabetic patients who may be candidates for transmetatarsal amputation.

The smaller group, which we will call Group I, consists of patients who have excellent arterial blood supply, but who have neuropathy or severe infections. The indication for surgery in these patients is either to get rid of a chronic or recurring ulcer beneath the forefoot or to reconstruct a foot after acute sepsis has destroyed portions of it—the definitive operation being accomplished, of course, after the active infection has been controlled by a combination of drainage and antibiotics as indicated. In many of these patients areas of gangrene develop due to local arterial thrombosis secondary to the infection.

The second and larger group consists of patients with arterial insufficiency in the involved foot. Usually there are no palpable pedal pulses, and other indications of arterial insufficiency are present. These patients have developed areas of skin necrosis on one or more toes, in the web space, or over the lateral aspect of the head of the first or fifth metatarsal. We have almost without exception discontinued amputating only the first toe and its metatarsal head for

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patients with ulcers overlying this area since a transmetatarsal amputation is more apt to heal and gives a more satisfactory foot. The plantar skin in this group of patients must be intact, and on the dorsum there must be no necrosis proximal to the metatarsal phalangeal joints. Transmetatarsal amputation is advised only when simple transphalangeal toe operations cannot be done due to the proximal location of the lesion or when more than one toe is involved.

OPERATIVE MANAGEMENT

Almost as important as the doing of the operation is the selection of the proper time to do it. This operation is not indicated as a means of getting ahead of an advancing process, but should be done only when the local condition is stabilized. In the group with arterial insufficiency this type of procedure will seldom be successful unless: (a) the necrotizing process has been localized by bed rest and conservative measures; (b) all active infection has been brought under control by rest, antibiotics, and surgical drainage, if indicated; (c) all rest pain has disappeared.

We frequently keep a patient in the hospital three weeks prior to surgery to accomplish these aims. Time beyond this will seldom produce further improvement. One can usually decide by three weeks whether or not an amputation through the forefoot is worth trying.

Technique.—With great care and gentleness incisions are made to create a thick plantar flap long enough to cover the end of the transected metatarsals. The dorsal incision is curved only slightly, and there is no dorsal flap as such since the circulation in this area would not support one. The metatarsals are cut just proximal to their heads and the ends are rongeured smooth. Primary closure is usually indicated in the arterial insufficiency group and is accomplished with fine No. 38 stainless steel wire skin sutures. In the group with good circulation, portions or all of the incision may be left open anticipating closure by secondary suture or skin grafting.

Postoperative Care.—A carefully padded plaster posterior splint is sometimes used to immobilize the ankle and foot in the more precarious cases. At all times before and after surgery the head is kept sufficiently elevated to assure filling of the veins of the foot and avoid blanching, as outlined by Buerger.[1]

The role of the antibiotics is important in many cases. Prior to surgery the lesion is cultured and the bacteria found are tested to see which antibiotic is the most effective. The appropriate agent can then be used pre- and postoperatively. Most commonly a combination of 600,000 units of penicillin and 1 Gm. of streptomycin is given daily. The broad spectrum antibiotics are employed (in standard doses of 1 Gm. per day) if indicated by the bacteriologic studies.

The sutures are left in for two to three weeks. If an occasional one appears too tight, it is removed. Weight-bearing is started very gradually, three to five weeks following operation in most cases. Most patients, when they are able to walk comfortably and bear full weight, wear a regular shoe with lambs' wool stuffed in the toes. A spring steel plate is inserted between the layers of leather in the sole to prevent curling up of the shoe.

FOLLOW-UP RESULTS

In all there were 433 transmetatarsal amputations of whom 67 were in the neuropathic-infection group and 366 in the arterial insufficiency group. There were 5 postoperative deaths, 68 immediate failures, and 360 initially successful operations (Table I).

TABLE I. TRANSMETATARSAL AMPUTATIONS

Group I (neuropathy-infection)	67	15.5%
Group II (arterial insufficiency)	366	84.5%
	433	
Postoperative deaths	5	1.2%
Initial success	360	83.0%
Early failure	68	15.8%
Total cases	433	

GROUP I. NEUROPATHY AND INFECTION

In these patients the circulation is excellent, and healing of the amputation eventually occurs in all the patients. Infection is the problem to contend with and may delay healing; in fact, in one case it did so for 117 days.

There were in all 67 patients in this group with ages ranging from 24 to 81 years (Table II). The average hospital stay (pre- plus postoperative) was 34 days. Our follow-up is complete on 57 of these patients whose operations were performed between 1944 and 1955 (Table III). At present 29 are alive and doing well. Twenty-two have died of causes not related to their feet. There was one postoperative death, and 5 late failures requiring higher amputation from 1 to 8 years after the initial operation.

A study of the follow-up returns showed that 44 of 47 patients who lived and were followed for 3 years following their amputations were doing well at that point. This is a 93.5 per cent "3-year cure." The results for the group alive 5 years or more showed that 31 of 34, or 91.2 per cent, were doing well at that time. Two patients required a higher amputation 7 and 8 years from the original operation. Several of the group have been using their partially amputated feet for 7 or 8 years successfully.

TABLE II. AGE AT OPERATION

YEARS	NEUROPATHIC	ARTERIAL INSUFFICIENCY
21-30	1	0
31-40	3	2
41-50	7	17
51-60	32	95
61-70	16	163
71 and over	8	89

TABLE III. GROUP I—RESULTS
(Neuropathy-Infection)

Died postoperatively	1
Died subsequently	22
Late failures	5
Lost	10
Currently successful	29
Total	67

GROUP II. ARTERIAL INSUFFICIENCY

There were 366 patients who had areas of gangrene due to deficient circulation. The average hospital stay was 46 days. Thirty-seven had bilateral

transmetatarsal amputations usually on different admissions.* The lowest palpable pulse was the aorta in 3, the femoral artery in 179, the popliteal in 162, and the dorsalis pedis or posterior tibial in 18. In 4 the pulse was not recorded.

In Table IV a comparison is made between the total group and the failures which shows a slightly lower percentage of palpable popliteal pulses in the unsuccessful cases.

TABLE IV. LOWEST PALPABLE PULSE
(Arterial Insufficiency Group)

LOWEST PULSE	TOTAL GROUP		EARLY AND LATE FAILURES	
Aorta	3	0.8%	1	0.8%
Femoral	179	48.9%	68	54.8%
Popliteal	162	44.4%	48	38.7%
Pedal	18	4.9%	5	4.0%
Not recorded	4	1.1%	2	1.6%
Total	366		124	

FOLLOW-UP RESULTS

The follow-up is complete on 348 of the 366 patients (95 per cent). At present 88 patients are alive and using the operated foot, 134 died after leaving the hospital, and 4 died postoperatively. One hundred twenty failed eventually, 2 are currently unhealed, and the fate of 18 is unknown (Table V). The times at which the failure occurred are of interest and are shown in Table VI.

TABLE V. RESULTS IN ARTERIAL INSUFFICIENCY GROUP

Postoperative deaths	4
Subsequent deaths	134
Failed	120
Unhealed currently	2
Lost	18
Alive and healed	88
Total	366

TABLE VI. FAILURE
(Arterial Insufficiency Group)

	NUMBER CASES
Postoperative deaths	4
Immediate failure (within 1 month)	68
Failure (less than 1 year)	6
Failure (1 year)	25
Failure (2 years)	6
Failure (3 years)	5
Failure (4 years)	3
More than 5 years	7
Total	124

In an effort to see how the transmetatarsal amputation stood up under everyday usage, the status of the patients in the group with necrosis due to deficient arterial supply was evaluated at three stages: 1, 3, and 5 or more years after surgery (Table VII). At the end of 1 year 317† patients were alive and of these 218 or 69 per cent were doing well. At 3 years 255† were alive and 156 were doing well, and at 5 or more years 174† were alive, of whom 87 were healed.

*Each operation was considered individually.
†Lost patients excluded.

TABLE VII. SUCCESSFUL OPERATIONS

TIME FROM OPERATION (YEARS)	TOTAL* PATIENTS	SUCCESSFUL RESULT	PER CENT
1	317	218	69
3	255	156	61
5 or more	174	87	50

*This represents the patients in the Total Group, i.e., 366 minus those who died after leaving the hospital or were lost. Thus the percentage of successes is lowered by both the early and late failures.

DISCUSSION

The Group I patients present little immediate problem. They are younger, have excellent circulation so that healing is the rule, and usually have brief hospital stays. The follow-up indicates that more than 90 per cent of these operations hold up well. Close supervision is essential through the years to guard against further ulcers in those with relatively numb feet. These patients are not long-lived due to the frequent accompanying renal, cardiac, and cerebral problems. In our series we learned that one-third of the patients had subsequently died from 1 to 8 years postoperatively.

In the arterial insufficiency group, the problem is more complicated. The decision as to whether a transmetatarsal amputation warrants a try is difficult. Much good judgment must go into this decision. If one had all good results, it might indicate too much conservatism in the selection of the patients at the expense of depriving some of operations that might be successful. In general, we hesitate to operate through the forefoot if rest pain cannot be controlled without narcotics, if there is much rubor on dependency, or if the venous filling time is over 25 seconds. Of course, exceptions are made occasionally. Successes were more frequent when a popliteal pulse was felt. However, its presence is not imperative as many successful operations were done without a palpable popliteal pulse and a few when even the femoral pulse could not be felt.

It will be noted that the operative mortality is low, but that the number of patients who die within a few years is great, reflecting their poor general condition. The opposite limb is frequently none too good and, in 48 of this group of patients, it had previously or subsequently been amputated.

Sympathectomy was performed on only 18 patients—none of whom were in Group I. The results cannot be evaluated accurately, but in general it seemed to help little unless there were clinical signs of vasomotor activity such as sweating or readily changing color or temperature levels.

When successful artery grafts have been accomplished, transmetatarsal amputations have been avoided.

The long-term survival of many of these amputations is gratifying. Once healed at the end of 1 year, only 21 subsequently failed. Several patients have kept trouble free for as long as 11 years.

SUMMARY

Among the 67 patients who had transmetatarsal amputation for neuropathy or infection (Group I) there were only 5 late failures requiring reamputation. Twenty-two of this group are known to be dead of causes not

related to this surgery, and 29 are known to be well and using the foot—many of them well beyond the 5-year period.

The arterial insufficiency group numbered 366, were older, and stayed longer in the hospital than Group I. Approximately one-third of these failed eventually. The incidence of failure was more closely related to the evaluation of the collateral circulation by the venous filling time and by other means than to the presence or absence of a popliteal pulse. Of course, only a few had pedal pulses. Sixty-one per cent of those who lived for 3 years had healed stumps at the end of that period, and 50 per cent of those who lived 5 years were similarly fortunate. The majority of failures occurred immediately postoperatively.

CONCLUSION

The transmetatarsal amputation has proved to be sufficiently successful and durable to indicate its continued use in diabetic patients properly selected. Unquestionably it has saved many limbs and has done so at little risk to the patient's life. Since frequently the longevity of the opposite leg is in question, efforts to be conservative in handling these problem cases are well worth while.

We would like to express our gratitude to Dr. Leland S. McKittrick for his help and guidance in preparing this paper.

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DISCUSSION

DR. EDWARD A. EDWARDS (Boston, Mass.).—I would like to comment briefly. I have seen one patient 84 years of age who had no pulse below the aorta, had diabetes, and polycythemia, and healed and did well for the three remaining years of his life after transmetatarsal amputation.

DR. ROBERT R. LINTON (Brookline, Mass.).—Drs. Wheelock, McKittrick, and their associates are to be complimented on the very excellent results of transmetatarsal amputations in this group of patients. It is easy to operate upon patients with good circulation since the incisions, almost as a rule, heal per primam, but it takes a tremendous amount of experience and judgment in doing this type of surgery in patients with poor arterial circulation. The circulation, instead of being a pulsatile flow through the arterioles, is more like a seepage under very low pressure so that even a tight skin suture may produce a slough with a disastrous result.

In dealing with these types of surgical wounds, one must have a different perspective than with routine abdominal or leg incisions where there is good circulation. For example, recently at our hospital on vascular rounds, a case was presented of a transmetatarsal amputation that had failed to heal despite a fairly good circulation. It was found that this patient had been discharged from the hospital to a nursing home 8 days after the procedure was performed. In my opinion such an early discharge from the surgeon's care is almost sure to result in a failure, as it did in this particular case, although at the time of discharge the incision appeared to be healing per primam. Fortunately such lessons as this are taken to heart and I am glad to say as a result of Drs. McKittrick's and Wheelock's precepts, the last successive 4 patients who had transmetatarsal amputation at our hospital have healed per primam, which is really a record.

THE EARLY REHABILITATION OF THE ARTERIOSCLEROTIC AMPUTEE

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RECENT advances in methods for reconstruction of arteries to the lower extremity obliterated by arteriosclerotic processes have given hope that the number of amputations of the lower extremity may be reduced. Recent reports of later closures of such reconstructive procedures of 50 per cent[5, 7] or 70 per cent[2] indicate, however, that it may be some time before this occurs. Lumbar sympathectomy has also failed to prevent amputation in many cases.[4] It seems certain, therefore, that until the obliterative process itself can be controlled, amputations will continue to be done for obliterative arterial disease.

Although the rehabilitation of the amputee with normal circulation has been widely discussed, the same is not true of the arteriosclerotic amputee. Many difficulties have arisen from applying the principles designed for the first group to the rehabilitation of the second. Loss of muscle tone and the desire to walk, unnecessarily severe contractures of joints, and lesions of the opposite foot occur too frequently during the treatment of the arteriosclerotic patient with an ischemic lesion of the lower extremity. It is the purpose of this paper to present a program of rehabilitation for the patient receiving an above-knee amputation for arteriosclerotic obliterative disease. Most of the principles set forth apply equally well to the patients before their amputations and to patients receiving other types of amputation in the lower extremity. The details which do not apply should be obvious. Implications as to which is the best amputation under given circumstances are not within the scope of the presentation. The program is intended to shorten hospital stay so that patients who may have only a few months or a year before another episode of arterial obliteration occurs can enjoy to the utmost the time remaining to them. Such a program, applied with enthusiasm and, above all, promptness, will often actually determine whether the patient ever walks again. The program is based on principles laid down 25 years ago by McKittrick.[3] Despite the amplification and modification of many details as outlined below, his basic principles and objectives have not been altered.†

Objectives to strive for:

A. Care and protection of the remaining foot.

B. Strengthening of the muscles necessary for walking.

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†Acknowledgment is also made to Drs. George W. vanGorder and Eugene E. Record for their teachings and to Drs. J. G. Bisgrove and Hart Achenbach for help with the case material.

C. Avoidance of flexion contracture of the hip on the amputated side.
D. Early provision of a temporary prosthesis.

A. *The Care and Protection of the Remaining Foot.*—

1. The remaining foot usually has impaired circulation and, in any case, will carry an extra load in walking. Pressure on vulnerable areas should be avoided, chiefly the external malleolus and the heel (Fig. 1, *a*). This

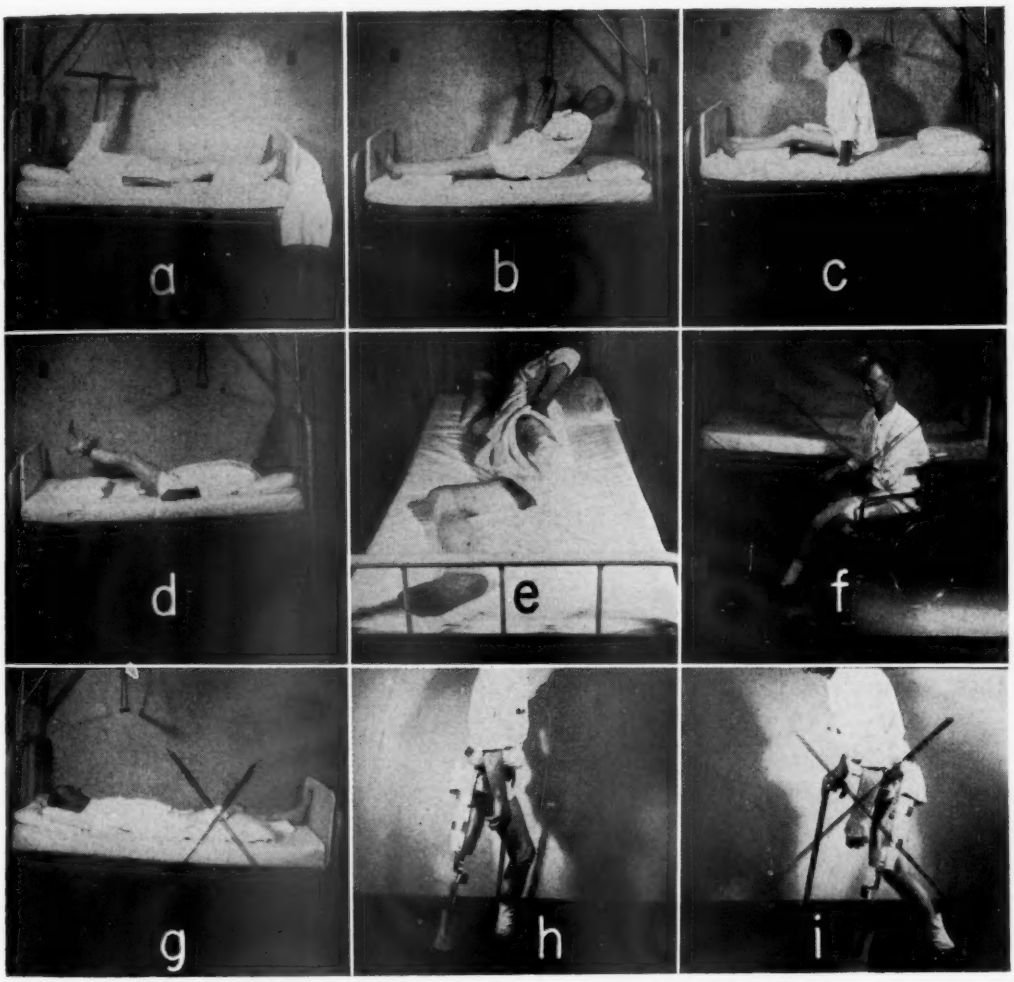

Fig. 1.—*a*, Position in bed showing overhead handles, pillow under calf of leg to keep heel off bed, and footboard; *b*, pull-up exercises; *c*, push-up exercises; *d*, exercise of well leg; *e*, hyperextension exercises of stump; *f*, don't have patient sit in early stages; *g*, don't place pillow under stump; *h*, correct method for first steps; *i*, incorrect method for first steps.

is accomplished by keeping a firm, flat pillow across the bed at the calf level, thus preventing contact of the foot with the bed.[3] Pads fastened to the foot, heel, or ankle are unsatisfactory. An overhead frame with handles or, if the patient is too weak, side bars to the bed should be provided in order to allow the patient to move himself about without using the remaining foot to push with. Elevation of the head of the bed is important to improve a severely

impaired arterial circulation in the remaining foot. It is not necessary if circulation is good and is not advisable during the first five postoperative days due to the recent amputation wound.

2. A footboard must be provided to keep the bedclothes from weighing on the foot (Fig. 1, *a*). Patients have damaged their feet by striking them against cradles placed over the feet. Cradles are therefore considered dangerous.

3. Daily foot care consisting of soap and water not warmer than 80° F., cleaning and trimming of the nails, drying of the foot, and application of lanolin is instituted on all feet except those with open or gangrenous areas.

4. Buerger's postural exercises are used as soon as they can be tolerated.[1, 3] Even if one has little confidence in one's ability to improve circulation in the remaining foot, these exercises keep a bed patient active, interested, and more able to care for himself.

5. It is of the greatest importance that the physician examine the remaining foot on his daily rounds. It happens too often that attention is directed solely toward the stump and its operative wound. Small areas of pressure or blistering can thus be detected and their causes corrected before permanent damage has occurred.

B. *Strengthening of the Muscles Necessary for Walking With a Prosthesis.*—

1. *The arms* are important since early training with a prosthesis will involve their vigorous use. Furthermore, if the patient is for some special reason to be recommended for crutch walking or a wheel-chair life, strong arms become increasingly essential. Arm strengthening is done by 5 or 10 pull-ups on overhead handles followed by 5 or ten push-ups from the sitting position 3 or 4 times a day (Fig. 1, *b* and *c*).

2. *The opposite lower extremity* is exercised by 5 or 10 bicycle exercises 3 times a day. Quadriceps setting and straight leg raising against resistance are done (Fig. 1, *d*). If the patient can stand, he should do so by the side of the bed with assistance and rock from heel to toe for a few moments twice a day. This can occur within 2 or 3 days after the amputation.

3. *The stump* is exercised as soon as wound pain has begun to diminish—namely, on the second or third day. The gluteal muscles and the adductors should be exercised against resistance.

C. Avoidance of Flexion Contracture of the Hip on the Amputated Side.—

1. Passive hyperextension should be instituted from the first postoperative day, and replaced by active hyperextension on the third day or sooner (Fig. 1, *e*).

2. The patient should lie on the abdomen 3 times a day for 20 minutes.

3. The sitting position should be avoided until the patient has shown that he is able to hyperextend his hip actively (Fig. 1, *f*).

4. A pillow should never be placed under the stump (Fig. 1, *g*). If elevation is needed, then the foot of the bed should be elevated.

D. *Early Provision of a Temporary Prosthesis.*—

1. The restoration of morale, the avoidance of bad walking habits, and the promotion of muscle development and of stump shrinkage make this a vital part of the program. As soon as amputation is decided upon, preferably before, the patient or his relatives should have a pair of the patient's everyday heavy duty shoes brought to the hospital. The limb maker is thus provided with a model for the artificial foot and the patient with a good shoe for walking with his remaining foot.

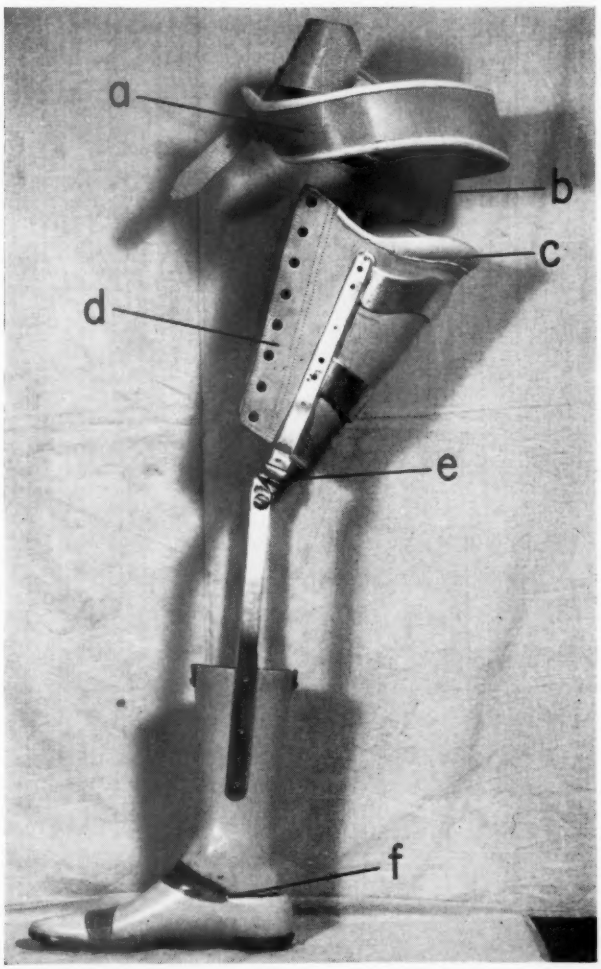

Fig. 2.—Temporary prosthesis showing: *a*, pelvic band; *b*, double-swivel hip joint; *c*, ischial seat; *d*, leather adjustable socket; *e*, ring lock knee joint; *f*, ball-bearing ankle joint.

2. Immediately after the amputation the limb maker is notified. He should make his measurements within 3 days of surgery. The measurements consist of (1) the length of the remaining limb, (2) the length of the stump, and (3) the circumference of the stump at three levels.

3. Since the making of the limb requires less than a week, a temporary prosthesis should reach the patient by the tenth postoperative day. If the stump heals per primam it should be possible to apply the temporary limb by the twelfth or fourteenth postoperative day. After a few days of gait training, it should be possible for the patient to go home before the twenty-first postoperative day without crutches, using two canes.

The Temporary Prosthesis (Fig. 2).—The type of temporary prosthesis recommended has an adjustable leather thigh socket which encloses the whole stump so that the end does not protrude below it. The socket has an ischial seat in order that all the weight may be borne on the ischial tuberosity. There is a manually operated lock knee joint with an artificial foot and ball-bearing ankle joint. The limb is held in place by a pelvic band which is connected to the thigh corset by a double-swivel hip joint. Rarely, a harness is needed if the patient's contour around the abdomen and hips is unsuitable for a pelvic band.

Responsibility for Rehabilitation.—An important part of the program is that the surgeon performing the operation be in charge of the rehabilitation of the patient. The ward personnel should be trained by him and supervised in the use of these measures. Once they have been instituted, they consume little time; but since they should be applied around the clock during waking hours, it is a matter which requires the supervision of the ward personnel rather than of a consultant or a consulting department.

If the rehabilitation is made the responsibility of services or specialties of the hospital other than that of the operating surgeon, the compelling drive toward early ambulation is often lost. These services have been accustomed to dealing with patients receiving amputations for traumatic, congenital, or neoplastic lesions. Such patients, not being hampered by generalized arteriosclerosis, can, without detriment to the end result, be rehabilitated at a more leisurely pace than the arteriosclerotic. In them, a more perfect fit of the prosthetic device and a perfect gait are more important. But if one strives for perfection of these points at the expense of extra days in the care of the arteriosclerotic, time lost is compounded not only by the initial delay but by the concomitant muscular wasting. The patient may, for this reason alone, never walk at all. Energetic opposition to such delaying influences, which went so far at one time in certain hospitals as to forbid the use of temporary prostheses, must frequently be exerted by the surgeon in order to accomplish his goal.

Gait Training.—Walking is initially accomplished by teaching the patient to stand and bear weight on the prosthesis. Considerable time spent at this can assure a proper fit of the prosthesis, a good balance, and the confidence of the patient.

In taking his first steps the patient, having first put all the weight on the amputated extremity, steps forward a few inches with the remaining foot (Fig. 1, *h*). In this and in the standing exercises mentioned, hand support may be gained from heavy furniture or parallel bars. After stepping forward with the remaining foot, the prosthetic foot is brought alongside by circumduction of the limb so that it will not strike the floor as it comes forward. It

should not be advanced beyond the other foot during early training, since it then acts as a strut or an obstruction to balance and to forward motion as the weight is put upon it (Fig. 1, *i*).

When confidence in fixed supports is gained, canes are used. Crutches are avoided at this stage. The patient should eventually graduate to one cane.

The patient should be taught stump bandaging so that he will wear an elastic bandage to shrink the stump when he is not wearing his limb. We have seen no contraindication to bandaging a stump with less than optimal arterial circulation. For the technique of bandaging, reference is made to Slocum.[6] We have usually omitted the spica element there depicted.

When the limb has been provided, the patient should wear it all the time he is out of bed. He should be taught to put it on and to take it off himself so that when he leaves he regards it as his new, efficient leg and not as a problem still to be surmounted.

Contraindications to the Use of a Limb.—The decision as to whether a given patient will be able to use a prosthesis is often difficult. It is urged only that it be made early by all the experienced heads available and carried forward with despatch and confidence. Contraindications to the use of a limb can be divided into two groups, those which also preclude crutch walking and those which will allow crutch walking. Included in the former are poor vision, hemiplegia with significant residual weakness, intercurrent disease, and senility. One of the most commonly considered contraindications is lack of motivation or desire on the patient's part. It is common, however, that an apparent lack of motivation can be altered in a patient who has an optimistic and confident adviser.

The contraindications to the use of a limb which permit crutch walking are a short, deformed, or unhealed stump and irreversible, severe hip flexion on the amputated side. The latter is nearly always due to neglect. Delay in walking will be necessary for an individual who has an unhealed stump of a major degree. Under these circumstances, however, crutch walking, though likely to cause bad gait habits, is better than no walking at all and should be advised until the stump is in condition. Since weight-bearing is on the ischial tuberosity, minor degrees of failure to heal, however, are not a contraindication to early use of the temporary prosthesis. Although crutch walking should never be allowed to be the preferred method during the early rehabilitation of the patient, it should be taught him *after* he has learned proper walking with his prosthesis and canes. It is a convenience to be able to use crutches as an emergency around the home without waiting to put on the leg.

Below-Knee Amputations.—Early rehabilitation of the below-knee amputee is as desirable as that for the above-knee. Since the presence of the knee joint makes walking, whenever undertaken, far easier, however, delays are not so costly as in the above-knee amputation. Although the below-knee temporary limb is somewhat similar to the permanent limb for the below-knee amputation in that a socket for the stump below the knee must be fashioned, ischial weight-bearing should be added to the prosthesis in the early period in order to avoid trauma to the stump. The importance of proper protection of the bony stump with stump socks cannot be exaggerated during this early phase.

Bilateral Amputees.—Although younger patients with bilateral above-knee amputations performed for traumatic lesions may be expected to walk on full length legs provided the stumps are good, this is not true of the arteriosclerotic group. Much physical strength in the muscles of the hip joints, the torso, and the upper extremities is needed, plus a degree of determination on the part of the patient. An occasional determined individual in the sixth decade or younger will accomplish it, particularly if the amputations have been widely enough spaced so that one permanent prosthesis has been perfectly mastered before the other limb is lost.

The usual prostheses provided for the arteriosclerotic receiving bilateral above-knee amputations are short pylons with leather thigh corsets and ischial weight-bearing. Although some individuals, for reasons of vanity, refuse to wear these limbs, most will welcome the independence it gives them as compared to the wheel chair and will do well with them. Short crutches are needed.

If the patient has an above-knee amputation on one side and a below-knee on the other, walking with full length prostheses can be expected due to the advantages of the preservation of one knee joint. This is particularly true if the amputations are done at separate times so that one of the prostheses can be adapted and used before both must be used together.

Later Management.—Since the purpose of the program is the *early* rehabilitation of the arteriosclerotic amputee, the later management, which centers around repeated checking and encouragement, weight control, and the provision of the permanent limb, will not be discussed. The permanent limb should be provided when maximum stump shrinkage has taken place, which usually happens between 3 and 6 months. It is to be mentioned, however, that some of the patients find that this "temporary" prosthesis satisfies their limited needs indefinitely and may not wish a permanent one.

RESULTS

A series of 41 above-knee amputations for obliterative arteriosclerosis performed at the West Roxbury Veterans Hospital and the Boston Veterans Hospital, First Surgical Division, over a period of 6 years was analyzed.

The average age of the patients was 61.2 years with a range from 48 to 80 years.

Nine (21.5 per cent) of the patients died postoperatively, 23 (57.0 per cent) used a prosthesis, and 9 (21.5 per cent) did not use a prosthesis. Thus, 71 per cent (23 out of 32) of the patients who survived were able to walk.

TABLE I. 41 ABOVE-KNEE AMPUTATIONS—REASONS FOR NOT USING PROSTHESIS

Previous contralateral amputation*	2
Senility	2
Arthritis	1
Poor vision	1
Hemiplegia*	1
Poor cooperation	1
Faulty rehabilitation	1
	9

*Not considered an absolute contraindication.

Table I shows the reasons that some did not use a prosthesis. In only one was faulty rehabilitation a cause, but this case alone will show that neglect on the part of the physician may make the difference between walking and not walking.

TABLE II. 23 ABOVE-KNEE AMPUTATIONS—INTERVAL FROM AMPUTATION OF WALKING WITH PROSTHESIS

2 patients	No information
21 patients—mean	6.5 weeks
18 selected patients*	4.3 weeks

*Patients unduly delayed, because of (1) fractured hip, (2) another unrelated operation, and (3) contralateral amputation, have been eliminated.

Table II shows that 21 patients who wore prostheses, on whom there was information, walked with a prosthesis an average 6.5 weeks after amputation. If one eliminates 3 patients who had great delays because of other intercurrent difficulties, the average time was 4.3 weeks. Since 4 of the patients walked well in 2.5 weeks postamputation, the average of 4.3 weeks is considered to be far above optimal. It is felt that with a more vigorous application of the program the average time of walking can be shortened. The main reasons for delay were the facts that the limb was procured late due to administrative delays and that vigorous rehabilitation of the patient's muscles had not been undertaken preoperatively and postoperatively.

SUMMARY

1. A program for the rehabilitation of the arteriosclerotic above-knee amputee has been presented.

2. Under this program 23, or 71 per cent, of a group of 32 patients surviving amputation walked with a prosthesis. In 18 selected patients the mean interval between amputation and walking with a prosthesis was 4.3 weeks. Four patients walked with prosthesis in less than 2.5 weeks postoperatively.

3. The application of this program, which requires the education of all personnel caring for the patient, can be rewarding in patient satisfaction, in shortened hospital stay, and in a lessened community responsibility for this group of patients.

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CHANGES IN COAGULATION OCCURRING IN DOGS DURING HYPOTHERMIA AND CARDIAC SURGERY

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HYPOTHERMIA has been shown to be useful in cardiovascular surgery. The reduction in metabolic rate provided by lowering body temperature to between 26° and 29° C. makes feasible the interruption of the circulation through the heart for 8 to 10 minutes. This interval of time is adequate for direct vision repair of some congenital cardiac anomalies.[2, 4, 19, 30, 31] In the surgical application of hypothermia, bleeding has been a significant problem.[14, 17, 21, 23, 28, 31] This bleeding usually occurs during rewarming and immediately thereafter. Management is especially difficult as the usual systemic manifestations of blood loss are masked by cooling alone.

To determine the cause of bleeding with hypothermia, a study of coagulation changes was undertaken. Although other reports[8, 10, 29, 33] on platelet count, clotting, bleeding, and prothrombin times have been made, these were limited to animals which did not undergo surgery. Animals for our study were subjected to open cardiac surgery with circulatory occlusion. Laboratory studies included hematologic values, clotting and bleeding times, prothrombin, prothrombin utilization, proaccelerin, proconvertin, fibrinolysin, and fibrinogen determinations.

METHODS

Coagulation studies were undertaken in dogs weighing 15 to 30 Kg. The animals were divided into 4 groups. Group A was composed of 4 animals which underwent the usual preparation for surgery including induction of anesthesia with thiopental sodium, external jugular vein cannulation, femoral artery cannulation, and intubation. Light anesthesia was maintained and the animals were hyperventilated for 6 hours with a Jefferson respirator.* One hundred per cent oxygen was used with a CO_2 absorption chamber. Positive and negative pressures were kept equal and varied from 5 to 7 cm. of water. The rate of respiration was maintained at 32 per minute and the inspiratory-expiratory time ratio was 1 to 1. Group B consisted of 4 animals which underwent the same preparation and hyperventilation but, in addition, were cooled to 26°-29° C. by immersion in ice water. After 2 hours of hypothermia, they were rewarmed by immersion in warm water. Group C consisted of 15 animals

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*Manufactured by Air Shields, Inc., Hartsboro, Pa.

which had the same preparation and hypothermia, plus open cardiac surgery. The procedure consisted of thoracotomy, 8 minutes of inflow and outflow circulatory occlusion, and creation of an interatrial septal defect. During thoracotomy the Jefferson respirator was adjusted to a positive pressure of 12 to 15 cm. water and negative pressure of 2 to 3 cm. water. Group D had the same preparation, hypothermia, and open cardiac surgery but were given intravenous heparin at the onset of cooling. This group consisted of 15 animals, 10 of which received 3 mg. of heparin per kilogram and 5 received 2 mg. per kilogram.

Fluid administration in the groups not exposed to surgery consisted of 500 ml. of electrolyte solution. In the groups undergoing surgery, it varied from 500 to 1,000 ml., depending on blood loss and the animal's size. No blood transfusions were given regardless of need, as this alone would have altered coagulation studies.

Blood samples were drawn as follows: Sample I was taken shortly after the induction of anesthesia and represents the normal for each animal. Sample II was drawn approximately 1.5 hours after Sample I, when hypothermia was reached in those undergoing cooling. After an interval of approximately 2 hours, Sample III was drawn and represents the maximum period of hypothermia in Groups B, C, and D. Surgery had just been completed in Groups C and D. Sample IV was taken 1.5 hours later, following rewarming of the hypothermic animals. The last sample, V, was drawn 1 hour later to detect latent changes after rewarming.

The surgical technique involved in the creation of an interatrial septal defect was similar to that described elsewhere.[16] The major portion of the interatrial septum was excised, creating a defect measuring 1.5 to 2.0 cm. in diameter. When ventricular fibrillation was encountered, it was treated with massage, epinephrine (1:10,000), and electric shock as indicated. A thoracotomy tube was left in the chest and aspirated frequently to determine blood loss. This was removed shortly after rewarming when the animal had begun to react. Thoracentesis was done postoperatively in any animal showing evidence of respiratory distress. Autopsies were performed in animals dying in the postoperative period and measurement of the amount of blood and fluid in the chest was made.

All laboratory studies included in this investigation were performed by the same technician utilizing methods which are standard in this laboratory. These techniques were as follows: (1) hemoglobin, as oxyhemoglobin,[1] (2) platelet count, indirect in Rees-Ecker diluent,[29] (3) clotting time, Lee and White at room temperature,[15] (4) bleeding time, Duke,[9] (5) prothrombin and proconvertin, Owren and Aas,[22] and (6) proaccelerin, Lewis and Ware.[18] Prothrombin consumption during 1-hour incubation of the blood sample at 37° C. was determined in the same manner as prothrombin. Fibrinogen was converted to fibrin by the action of 10 units of bovine thrombin on an appropriately diluted and recalcified plasma sample (1.0 ml.). The fibrin was then quantitated by the usual biuret method. Blood clots were observed during a 24-hour incubation at 37° C. for the presence of excess fibrinolysin.

RESULTS: LABORATORY STUDIES

Group A.—This group underwent all preparation for surgery as well as 6 hours of hyperventilation. Table I shows the mean values for the 4 animals of this group. It will be seen that the platelet count steadily decreased from 451,000/cu. mm. at the beginning (Sample I) of the procedure to 259,300/cu. mm. at the end of the 6-hour interval (Sample V). Proaccelerin, proconvertin, and prothrombin always began at 100 per cent as Sample I was considered to be the standard with which other samples were compared. All of these factors are seen to decrease only slightly during the procedure. Hemoglobin and fibrinogen did not undergo significant change in this group. The clotting time showed a tendency to shorten and the bleeding time was variable.

TABLE I. MEAN VALUES OF 4 ANIMALS IN GROUP A UNDERGOING PREPARATION FOR SURGERY AND 6 HR. OF ANESTHESIA PLUS HYPERVENTILATION

SAMPLE	HEMOGLOBIN GM. %	PLATELETS /CU.MM.	PROACCELERIN PER CENT	PROCONVERTIN PER CENT	PROTHROMBIN PER CENT	FIBRINOGEN MG. %	CLOTTING TIME IN MINUTES	BLEEDING TIME IN MINUTES
I	12.9	451,000	100	100	100	295	9.3	1.5
II	12.9	340,000	94	98	97	*	8.0	1.8
III	11.9	302,000	91	95	97	240	6.5	1.5
IV	12.7	289,500	91	88	96	*	4.5	1.0
V	12.5	259,300	92	86	96	305	4.6	0.9

*No determinations made on these samples.

Group B.—This group of 4 animals underwent the same preparation plus hypothermia. As seen in Table II the platelet count mean followed a different pattern in this group. With cooling (Sample II) the count dropped from the original value of 493,800/cu. mm. to 236,900/cu. mm. A further drop to 134,900/cu. mm. occurred after 2 hours of hypothermia. With rewarming there was a progressive increase finally reaching a value slightly higher than that of Sample I. The hemoglobin means showed an increase from 11.9 Gm. per cent at Sample I to a maximum of 14.7 Gm. per cent after 2 hours of hypothermia (Sample III). There was a tendency for the hemoglobin values to return to normal with rewarming although this was not complete at Sample V. Proaccelerin, proconvertin, and prothrombin decreased from 100 per cent to 47 per cent, 69 per cent, and 67 per cent, respectively, at Sample V. The fibrinogen followed the same pattern, dropping from an initial value of 347 mg. per cent to 280 mg. per cent at Sample V. Clotting and bleeding times were variable.

TABLE II. MEAN VALUES OF 4 ANIMALS IN GROUP B UNDERGOING PREPARATION FOR SURGERY AND HYPERVENTILATION PLUS COOLING TO 26°-29° C.

SAMPLE	HEMOGLOBIN GM. %	PLATELETS /CU.MM.	PROACCELERIN PER CENT	PROCONVERTIN PER CENT	PROTHROMBIN PER CENT	FIBRINOGEN MG. %	CLOTTING TIME IN MINUTES	BLEEDING TIME IN MINUTES
I	11.9	493,800	100	100	100	347	8.5	0.6
III	14.4	236,900	82	93	95	*	9.9	0.9
IV	14.7	134,900	78	82	90	*	8.1	1.1
II	14.2	309.500	80	86	84	293	6.5	0.9
V	13.9	513,900	47	69	67	280	7.9	1.0

*No determinations made on these samples.

Group C.—Group C had the same preparation and cooling as Group B but in addition underwent circulatory occlusion and open cardiac surgery. Table III shows the means of 15 animals included in this study. The platelet change was similar to Group B with a decrease from 355,500/cu. mm. at Sample I to 151,600/cu. mm. after 2 hours of hypothermia (Sample III). One hour after rewarming, the count had returned to 398,800/cu. mm. The hemoglobin increased from 12.8 Gm. per cent at Sample I to 15.7 Gm. per cent at Sample III. As in Group B, there was a tendency for the hemoglobin to return to normal with rewarming. Proaccelerin, proconvertin, and prothrombin decreased more severely in this group, reaching 33 per cent, 58 per cent, and 67 per cent respectively at Sample V. The fibrinogen decreased progressively from 434 mg. per cent (Sample I) to 289 mg. per cent (Sample V). The clotting time progressively shortened, beginning at 7.1 minutes and ending at 3.1 minutes. The bleeding times did not follow a definite pattern.

TABLE III. MEAN VALUES OF 15 ANIMALS IN GROUP C UNDERGOING HYPOTHERMIA PLUS 8 MINUTES OF CIRCULATORY OCCLUSION AND OPEN CARDIAC SURGERY

SAMPLE	HEMOGLOBIN GM. %	PLATELETS /CU.MM.	PROACCELERIN PER CENT	PROCONVERTIN PER CENT	PROTHROMBIN PER CENT	FIBRINOGEN MG. %	CLOTTING TIME IN MINUTES	BLEEDING TIME IN MINUTES
I	12.8	355,500	100	100	100	434	7.1	1.2
II	15.9	232,200	83	97	94	*	8.8	1.0
III	15.7	151,600	53	81	81	317	5.8	1.2
IV	14.5	270,700	37	68	71	*	4.6	1.1
V	14.3	398,800	33	58	67	289	3.1	0.8

*No determinations made on these samples.

TABLE IV. MEAN VALUES OF 15 ANIMALS IN GROUP D UNDERGOING HYPOTHERMIA AND CARDIAC SURGERY BUT RECEIVED HEPARIN JUST PRIOR TO COOLING

SAMPLE	HEMOGLOBIN GM. %	PLATELETS /CU.MM.	PROACCELERIN PER CENT	PROCONVERTIN PER CENT	PROTHROMBIN PER CENT	FIBRINOGEN MG. %	CLOTTING TIME IN MINUTES	BLEEDING TIME IN MINUTES
I	11.6	411,900	100	100	100	330	9.1	1.4
II	*	*	†	†	†	†	>120.0	7.1
III	15.3	348,800	†	†	†	†	63.9	3.4
IV	13.3	388,200	56	69	78	252	14.3	2.0
V	12.9	444,700	64	76	80	254	6.9	1.6

*No determinations made on these samples.
†Determinations technically impossible because of high titer of heparin.

Group D.—This group differs from Group C in that heparin was given just prior to cooling. Table IV shows the mean values of 15 animals in this group. The platelet count shows only a slight change, dropping from 411,900/cu. mm. (Sample I) to 348,800/cu. mm. (Sample III) after 2 hours of hypothermia. Upon rewarming, the count increased to reach a higher value at Sample V than Sample I Proaccelerin, proconvertin, and prothrombin decreased to 64 per cent, 76 per cent, and 80 per cent, respectively. Fibrinogen decreased from 330 mg. per cent at Sample I to 254 mg. per cent at Sample V. Hemoglobin values show an increase from 11.6 Gm. per cent at Sample I to 15.3 Gm. per cent at Sample III. After rewarming, the hemoglobin returned to 12.9 Gm. per cent (Sample V). Clotting times were greatly altered by the

use of heparin. The first 10 animals of this group received 3 mg. per kilogram while the last 5 were given 2 mg. per kilogram. A comparison of the clotting times of these 2 subgroups may be seen in Fig. 1. It is seen that at Sample II both clotting times were above 2 hours. At Sample III the clotting time was 75.6 minutes in the 3 mg. group and 42.8 minutes in the 2 mg. group. In both groups the clotting times decreased progressively to approach normal at Sample V. The bleeding times showed an increase to 7.06 minutes at Sample II when the effect of heparin was maximum. This progressively decreased to approximate normal at Sample V.

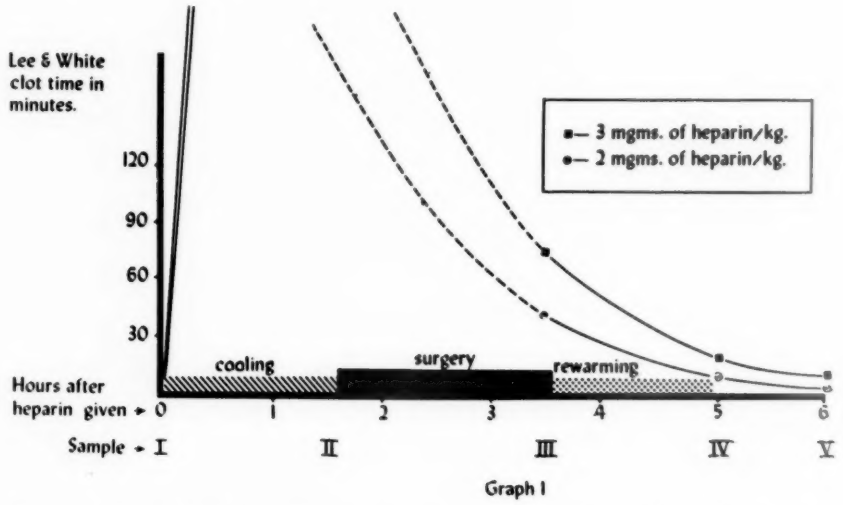

Fig. 1.—Comparison of clotting times in dogs receiving 2 mg. and 3 mg. of heparin per kilogram.

BLOOD LOSS AND MORTALITY

In Groups A and B which did not undergo surgery, the blood loss consisted of 200 ml. drawn for samples. There was no mortality in either of these groups. In Group C an additional loss was incurred with thoracotomy. Care was taken to provide good hemostasis while the chest was open and no measurement was made of the blood loss during the procedure. After closure, a careful evaluation of blood loss into the chest was made by frequent aspiration of the chest catheter. The mean of the measured blood loss during the procedure in the 15 animals of Group C was 270 ml. Of this group 10 animals were alive after Sample V. Of these 10 animals 6 had direct evidence of bleeding in the first 48 hours postoperative as shown by post-mortem examination or thoracentesis.

The mortality of the 15 animals in Group C at the end of the procedure was 33.3 per cent (5 animals). Two of these animals died suddenly with the removal of the venous catheter. In animal No. 2 a large ante-mortem clot was found in the main pulmonary artery. Following this mishap, catheters were withdrawn with careful aspiration to remove any attached clots. In several animals, an extensive clot was removed from the catheter thus preventing an embolus. In spite of this precaution, one animal (No. 8) died suddenly with the removal of the catheter. No embolus was found at necropsy in the pulmonary artery but an interatrial septal defect had been created and a cerebral

embolus could not be excluded. One animal which began the procedure with a white count of 37,000/cu. mm. died during rewarming. This animal was found to have severe pneumonia. Two animals died during rewarming without obvious cause of death. The right ventricle was significantly dilated in both these animals. Six animals died during the first week after surgery, increasing the mortality to 73.3 per cent. The chest was opened after death in all animals except No. 10 and atelectasis was found, usually associated with some degree of hemorrhage. (See Table V.) Right ventricular dilation was also present in most of these animals.

TABLE V. SHOWING BLOOD LOSS AND MORTALITY OF 15 ANIMALS IN GROUP C

PROCEDURE NUMBER	TOTAL BLOOD LOSS SAMPLES I-V IN C.C.	PROVED BLOOD LOSS FIRST 48 HOURS IN C.C.	COMMENTS
1	400	200	Died 12 hr. postop.; cause of death uncertain; 200 c.c. blood in chest
2	450	---	Died suddenly with removal of venous catheter (pul. embolus)
3	200	None	Died 48 hr. postop.; cause of death uncertain; moderate atelectasis
4	200	---	Died with rewarming; severe pneumonia present preoperatively
5	400	600	Died 12 hr. postop.; 600 c.c. blood in chest
6	250	300	Survival thoracentesis 48 hr. postop. revealed 300 c.c. blood in chest
7	300	300	Died 12 hr. postop.; cause of death uncertain, 300 c.c. blood in chest
8	200	---	Died suddenly with removal of venous catheter
9	320	None	Died 12 hr. postop.; cause of death uncertain; moderate atelectasis
10	200	200	Died 72 hr. postop.; thoracentesis at 48 hr. revealed 200 c.c. blood; no autopsy
11	200	None	Survival
12	200	200	Survival thoracentesis 2 days postop. revealed 200 c.c. blood
13	225	---	Died during rewarming; cause of death uncertain
14	200	None	Survival
15	300	---	Died during rewarming; cause of death uncertain

TABLE VI. SHOWING BLOOD LOSS AND MORTALITY OF 15 ANIMALS IN GROUP D

PROCEDURE NUMBER	TOTAL BLOOD LOSS SAMPLES I-V IN C.C.	PROVED BLOOD LOSS FIRST 48 HOURS IN C.C.	COMMENTS
1	225	None	Survival
2	275	None	Survival
3	275	None	Survival
4	205	None	Survival
5	120	None	Survival
6	140	None	Survival
7	1150	---	Died during rewarming; severe hemorrhage
8	325	None	Survival
9	475	30	Died 12 hr. postop.; bled excessively with rewarming
10	375	None	Survival
11	175	None	Survival
12	305	None	Survival
13	130	None	Survival
14	130	None	Survival
15	210	None	Survival

The blood loss and outcome of Group D are shown in Table VI. The mean blood loss during the procedure (from Sample I to Sample V) was 300 ml. This included blood drawn for samples and bleeding into the chest occurring with rewarming. Although only 80 ml. of blood was drawn for samples in each dog of this group, the bleeding during rewarming was slightly greater. Surgical blood loss was not measured but was estimated as being slightly more in this group than in Group C. Fourteen animals were alive after Sample V. One of these was shown to have an insignificant amount (30 ml.) of blood in the chest by post-mortem examination. None of the other 13 animals showed any evidence of respiratory distress during the first 48 hours after surgery to warrant thoracentesis. It is assumed that none of these animals had significant bleeding into the chest after Sample V.

One animal in Group D died during the procedure, making the mortality 7 per cent. Excessive bleeding occurred after closure of the chest and during rewarming. This probably represents a hypersensitivity to heparin, as the clotting time did not follow the usual pattern. At Sample III the clotting time was over 2 hours whereas the mean value for the group was 63.9 minutes. Another animal of this group died 12 hours postoperatively, increasing the mortality to 13 per cent. This animal likewise had an unusually severe response to heparin with the clotting time again greater than 2 hours at Sample III. Bleeding was excessive during rewarming, and it is probable that this contributed to the animal's death.

DISCUSSION

Coagulation changes have been studied during hypothermia and open cardiac surgery. It was observed that the prothrombin utilization was adequate in all groups. Furthermore, no fibrinolysin was detected in any of the groups. A comparison of proaccelerin, proconvertin, prothrombin, and fibrinogen changes occurring in the 4 groups is shown in Table VII. This shows the mean values for the coagulation factors which were present at the conclusion of the procedure (Sample V). These values are expressed as a per cent of normal (100 per cent). The mean blood loss per kilogram and the mean per cent change in hemoglobin are also represented. It is seen that the blood loss per kilogram during the procedure did not vary a great deal in these groups. There was a hemoconcentration in all groups undergoing cooling although fluid was administered in excess of blood loss. This suggests that the depletion of the various coagulation factors was not a manifestation of hemodilution. It is seen that in Group A only minimal changes occurred in proaccelerin, proconvertin, prothrombin, and fibrinogen. With the addition of hypothermia (Group B), a significant drop in these factors was seen to occur. The decrease was even greater with the addition of surgery (Group C). We believe that the depletion of these factors is the result of intravascular clotting. This is similar to a process described by Schneider[25-27] in patients with abruptio placentae. He reported the release of tissue thromboplastin by the placenta, resulting in an acceleration of the clotting process. With subsequent intravascular clotting

there was a depletion of proaccelerin, proconvertin, prothrombin, and fibrinogen. During hypothermia, the cause of intravascular clotting could be attributed to several factors. The cardiac output decreased[12] and the velocity of blood flow is reduced. There is a marked hemoconcentration which increases the viscosity of the blood.[8, 10, 11, 13, 14, 32, 33] A decrease in platelet count[6, 14, 32, 33] is known to occur with hypothermia. If this is attributable to platelet destruction, a release of platelet thromboplastin would occur, precipitating intravascular clotting. In those animals undergoing surgery the circulatory stasis resulting from inflow and outflow occlusion would favor coagulation.[34] Furthermore, trauma to the lungs, a known source of thromboplastin,[3] may result in the release of tissue thromboplastin into the blood stream.

The mortality and blood loss occurring in Group C, which had the greatest depletion of coagulation factors, provides evidence of intravascular clotting. Two animals died suddenly with the removal of the venous catheter, and a pulmonary embolus was demonstrated in one. It is believed that the other animal died from a cerebral embolus reaching the left side of the heart through an interatrial septal defect. Furthermore, several animals of this group died without obvious cause. These animals were found to have a dilated right ventricle at necropsy. This finding has been reported in association with an increase in pulmonary arterial pressure resulting from pulmonary emboli. Sections of lung were preserved for microscopic study in only 3 animals. One of these (Group C—animal No. 4) died of severe pneumonia during rewarming, and microscopic study showed only this process. Two animals (Group C—animals Nos. 2 and 5) were found to have microscopic evidence of clots in pulmonary vessels (Figs. 2 and 3). It was not possible to determine if these were embolic or thrombotic in nature.

Aside from the problem of thromboembolic phenomenon associated with intravascular coagulation during hypothermia and surgery, a serious depletion of coagulation elements may occur (Table VII). This produces a clotting defect which results in postoperative hemorrhage with rewarming and restoration of blood pressure. Evidence of this hazard is seen in Table V which shows the blood loss in Group C during the first 48 hours postoperatively. It is seen that 60 per cent of the animals surviving the procedure had evidence of significant bleeding during this period.

TABLE VII. THIS SHOWS THE MEANS OF THE BLOOD LOSS AND OF THE PER CENT CHANGE WHICH HAD OCCURRED IN THE COAGULATION FACTORS AT THE CONCLUSION OF THE PROCEDURE (SAMPLE V)

GROUP	WEIGHT IN KG.	TOTAL BLOOD* LOS IN C.C.	BLOOD LOSS/ KG.*	HEMO-GLOBIN PER CENT	PRO-ACCELERIN PER CENT	PRO-CONVERTIN PER CENT	PRO-THROMBIN PER CENT	FIBRIN-OGEN PER CENT
A	18	200	11.2	98	92	86	96	105
B	12.8	200	15.7	119	47	69	67	80
C	21.8	272	12.8	112	33	58	67	59
D	19.1	245	12.7	113	64	76	80	77

*This is the blood loss in those animals surviving at Sample V.

It will be noted in Table III that, despite the depletion of proaccelerin, proconvertin, prothrombin, and fibrinogen factors in coagulation, the Lee and

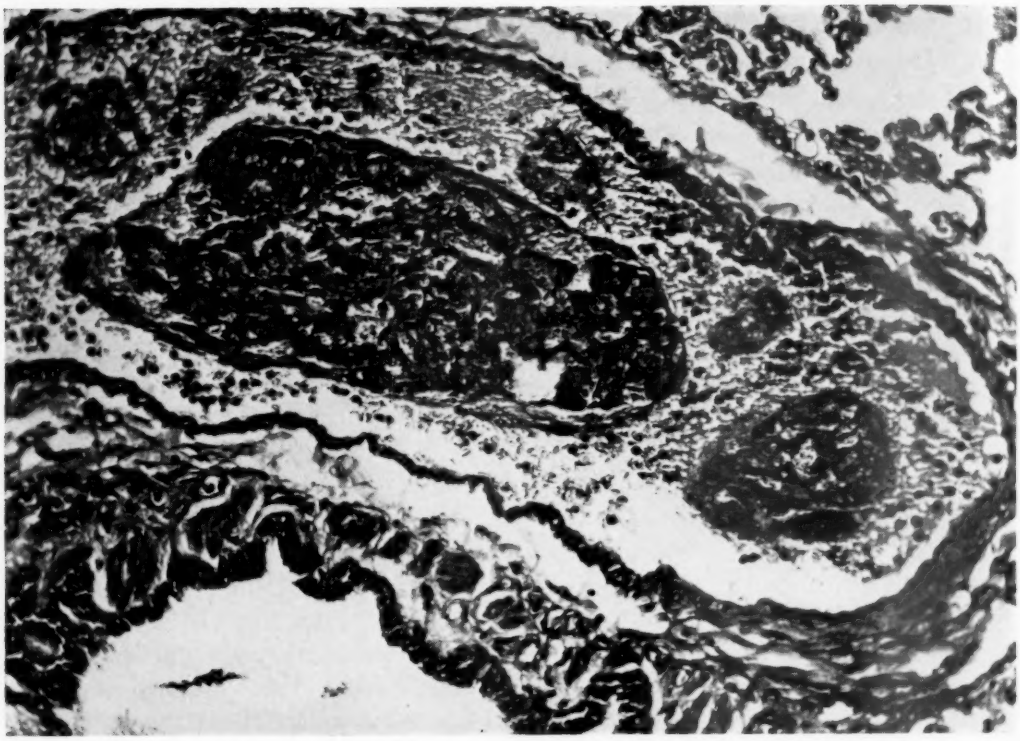

Fig. 2.—Group C, animal No. 2. This shows thromboembolism within a pulmonary vessel adjacent to a bronchiole.

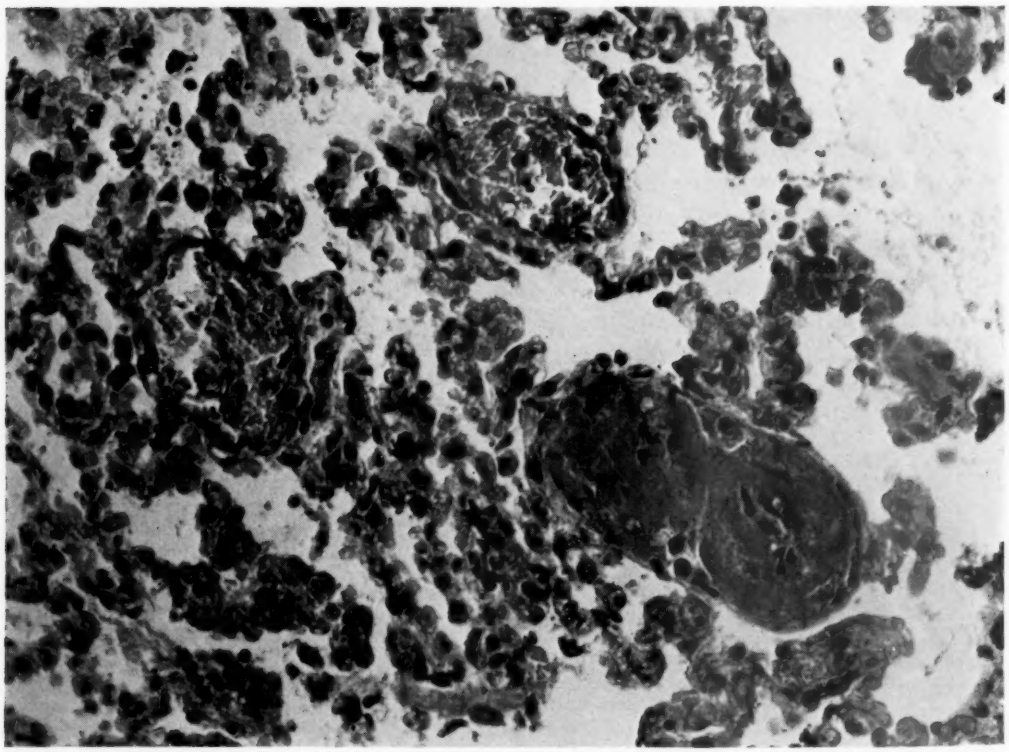

Fig. 3.—Group C, animal No. 5. This shows complete occlusion of a small pulmonary vessel by thromboembolism.

White clotting time is actually shortened. This serves to demonstrate the well-known fact that the Lee and White clotting time is independent of prothrombin, proaccelerin, and proconvertin if these factors are present in concentrations at a level of 25 per cent of normal. Actually the percentage values of all four factors were well above the critical level. The clotting time is more dependent on the concentration of thromboplastin factors which was normal during this procedure. Thus, the short clotting time in this group is compatible with this depletion of the coagulation factors by intravascular clotting.

Heparin has been shown[5, 7] to be effective in inhibiting intravascular clotting resulting from a variety of physiologic disturbances. Group D demonstrates the effectiveness of heparin in the inhibition of this process during hypothermia and open cardiac surgery. As seen in Table IV the depletion of proaccelerin, proconvertin, prothrombin, and fibrinogen was less severe after the use of heparin. In addition, the transient drop in platelet count which may be associated with intravascular clotting[27, 34] was greatly inhibited by the use of heparin. A comparison of the change in platelet counts occurring in Group C and Group D may be seen in Fig. 4.

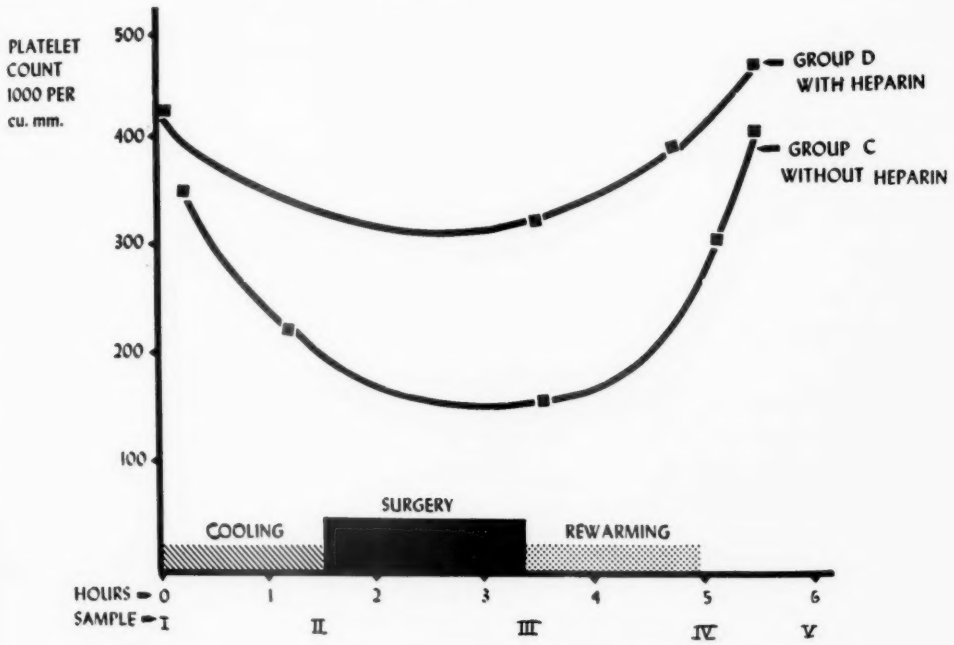

Fig. 4.—Showing change in platelet counts of Groups C and D.

The mortality associated with hypothermia and cardiac surgery was greatly reduced by the use of heparin (Table VI), and there were no deaths in this group attributable to pulmonary emboli. Furthermore, hemorrhage after rewarming was insignificant.

We believe that the process of intravascular clotting probably occurs to some degree in all animals undergoing hypothermia and cardiac surgery. The extent to which it occurs varies with each individual animal. Those animals

which experience only minimal degrees of clotting may fail to manifest symptoms. Heparin seems effective in minimizing the process and avoiding its complications.

The use of heparin during hypothermia and cardiac surgery is not without hazard. There is a marked prolongation of the clotting time for a period of 5 to 6 hours during which time surgery must be accomplished. We have found bleeding during surgery with heparin to be easily controlled. This was especially true in those animals receiving 2 mg. per kilogram. Bleeding was excessive during rewarming in 2 animals, both of which had received 3 mg. of heparin per kilogram. In evaluation of the clotting time response, it seems probable that these 2 animals had a diminished tolerance to heparin. At the present time we are evaluating various methods of determining heparin tolerance preoperatively to prevent overdosage. Furthermore, an overdosage might be neutralized with protamine sulfate during the rewarming period, should the bleeding be excessive.

SUMMARY

1. Coagulation changes have been studied in dogs undergoing hypothermia and cardiac surgery.

2. A depletion of proaccelerin, proconvertin, prothrombin, and fibrinogen was found to occur. We believe that this results from intravascular clotting.

3. Intravascular clotting predisposed to the dangers of thromboembolic phenomenon. Several deaths occurred with hypothermia and cardiac surgery which are believed to be attributable to pulmonary emboli.

4. Furthermore, intravascular clotting depleted the blood of certain factors necessary for coagulation resulting in a clotting defect. Hemorrhage after rewarming was a significant problem in those animals undergoing hypothermia and cardiac surgery.

5. Heparin was given intravenously to inhibit intravascular clotting. The depletion of coagulation factors was minimized. None of these animals showed evidence of thromboembolic phenomenon and the mortality was greatly reduced Furthermore, no post-rewarming hemorrhage occurred.

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DISCUSSION

DR. W. G. BIGELOW (Toronto, Ont.): I would like to say that I think hemorrhage is becoming one of the important problems in the clinical application of hypothermia. I would like to encourage the essayists to keep up their work and tell us as much about this problem as they can because it has been a source of worry to us. We have, in the last

year, had a biochemical team working on our clinical cases, both as an adjunct and with interruption of the circulation, and we suspect the calcium and citrate mechanisms as being at least one of the factors, and perhaps of some importance.

We are studying the reason why the calcium should go down and the citrate should go up to remarkably high levels. It is unfortunate that they are difficult things to measure. In Toronto and London, England, we are finding a metabolic acidosis during the rewarming period, which I think is an integral part of this picture.

I must say, if for no other reason than to warn those who are embarking on hypothermia, this is a real problem. We do not know the answer. As you lower the body temperature, you are interfering with a very complex system of biochemical reactions, and it is a further reason why we should not lower the body temperature much below 30° or 28° C.

DR. CECIL M. COUVES (Houston, Tex.): We, too, have been interested in the hematologic changes which result from cooling both in humans and in the experimental animal. I would like to present some of our experimental results in the dog.

(Slide 1.) We have measured the coagulation time in 40 dogs with various depths of hypothermia down to 20° C. These were measured in glass and you can see they are not significantly altered. Subsequent studies carried out in silicone tubes show some prolongation of the coagulation times at reduced temperatures.

You will notice that the bleeding times almost consistently show a five- to sevenfold increase at the depth of cooling. Along with most people, we have found that the hemoglobin and hematocrit values increase with cooling. Our prothrombin times in plasma were not altered significantly by cooling, but the prothrombin times in serum were shortened, indicating considerable residual prothrombin.

The platelet count drops precipitiously with cooling, and with this, clot retraction is poor. The leukocytes also fall. We could find no alterations in the osmotic or mechanical fragility, nor was the critical fibrinogen index changed. Likewise, the heparin activity at these reduced temperatures was not significantly changed.

DR. LE ROY J. KLEINSASSER (Closing): I would like to comment that hypothermia represents a very complex situation in which a great number of experiments have been done by us, including the evaluation of the metabolic acidosis that these individuals undergo. Certainly, of the complications that develop, those of ventricular fibrillation and the problem of coagulation are the most difficult. Although obvious in the experimental animal, the clinical use of heparin in the treatment of a patient during hypothermia is a matter we have not investigated. On the basis of these studies, we feel its use during hypothermia should be seriously considered.

DEFIBRILLATION, CARDIAC ARREST, AND RESUSCITATION IN DEEP HYPOTHERMIA BY ELECTROLYTE SOLUTIONS

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(From the Department of Surgery, University of Maryland School of Medicine)

ACCESSIBILITY to the cardiac chambers during heart surgery is the factor which will determine the extent of further hypothermia utilization in this field. To achieve and prolong the desired cardiac chamber accessibility, greater cooling is needed to reduce the body metabolic requirements. In addition, some type of control must be exerted over all cardiac activities which can and will effect a normal heartbeat after a prolonged period of ventricular fibrillation or cardiac standstill.

This paper reports experiences with 47 dogs whose body temperatures were reduced to within a range of 29° to 15° C. and who were then deliberately fibrillated by electrical stimulation. Normal cardiac rhythm was then restored with the use of electrolyte solutions combined with cardiac massage.

METHODS AND MATERIALS

Mongrel dogs, weighing from 12 to 40 pounds, were anesthetized with intravenous Nembutal sodium, ventilated by 100 per cent, and cooled by emersion in iced water. After the desired body temperature level was reached, a left thoracotomy was made and ventricular fibrillation was induced by direct electrical stimulation to the heart. Immediately following ventricular fibrillation potassium chloride solution, 15 per cent, varying in quantity (1 to 3 c.c.), according to individual animal body weight, was injected into the left ventricle and forced through the coronary arteries by slow manual massage. In order to remove excess potassium chloride, to restore myocardial tone, and to adequately oxygenate the myocardium, massage was continued for a minimum time period of 20 seconds. As a result of the potassium chloride injection followed by massage, defibrillation occurred in 25 per cent of the animals within a 6-second interval. In 50 per cent of the animals, defibrillation occurred within 12 seconds following this procedure, and in the remaining group of 25 per cent, defibrillation occurred in 45 seconds (Fig. 1). Transient cardiac standstill, occurring in 5 dogs following potassium chloride administration, spontaneously returned to normal rhythm. Such spontaneous remissions have been previously described by Swan and his associates.[13]

Following defibrillation, cardiac resuscitation measures were initiated. Electrical activity in the myocardium was re-established with the use of sodium lactate solution and coordinated beats were induced with the use of Ringer's

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lactate. Slow, gentle, manual massage prevented and also overcame cardiac chamber distention. When the myocardial tissue appeared well oxygenated, 2 or 3 c.c. of sodium lactate (10 per cent solution)* was injected into the left ventricle while massage was continued. Within seconds myocardial electrical activity usually returned (Figs. 2, 3, 4, and 5). Column 2, in Fig. 1, shows that electrical activity returned in 29 per cent of the animals after injection of sodium lactate within a period of 6 seconds. In an additional 44 per cent, the electrical activity was present on electrocardiograms within 12 seconds and in the rest, in 45 seconds.

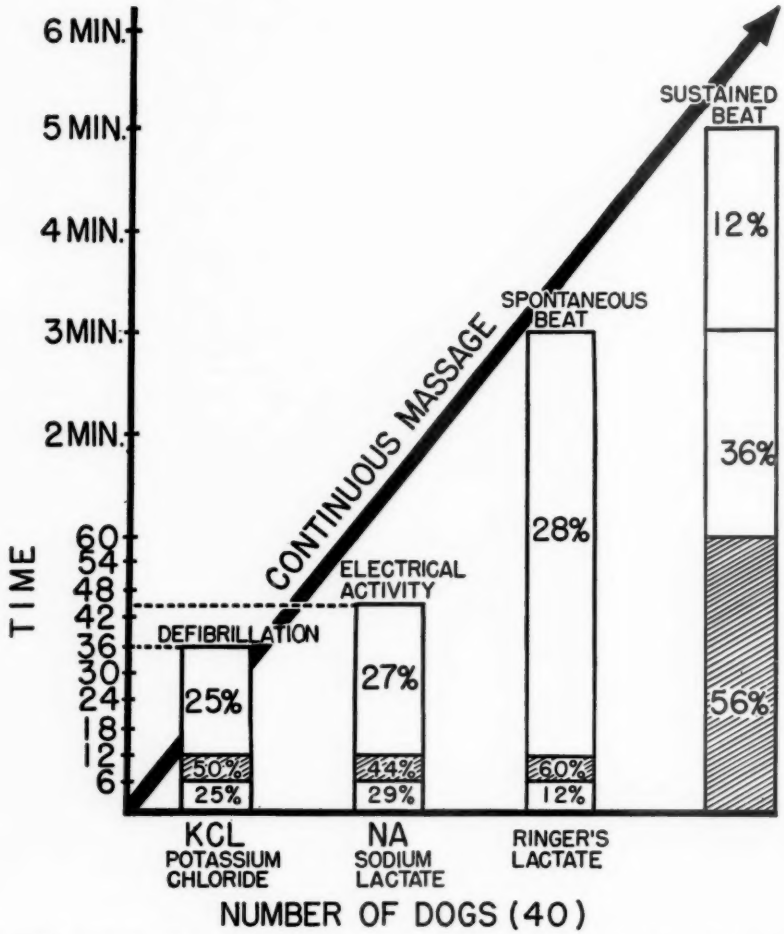

Fig. 1.—The relationship of time and the effect of electrolytes and cardiac massage in defibrillation and resuscitation during deep hypothermia.

Coordinated effective cardiac contractions were established by the injection of 2 to 3 c.c. of Ringer's lactate (25 times concentrated)† into the left ventricle. Cardiac massage was continued until contractions became regular and sustained. While the first spontaneous contractions were usually felt by the operator within 12 seconds, the achievement of an effective heartbeat sometimes required as much as 5 minutes of assisting massage. In the event of

*Parke, Davis & Company.
†Eli Lilly and Company.

cardiac dilatation and sluggish, feeble contractions, a slow intravenous drip of 10 c.c. of 10 per cent calcium gluconate in 200 c.c. of 5 per cent dextrose in water was started. As quickly as myocardial tone was established, the infusion of calcium gluconate was stopped, since excessive calcium can often precipitate ventricular fibrillation and should be used with caution.

After reaching and maintaining normal cardiac rhythms, the dogs were rewarmed with heating pads. The thoracotomy was closed after the animals' body temperatures reached 25° C. and regular sinus rhythm was present on the electrocardiogram. On reaching 34° C. the animals were disconnected from the respirator.

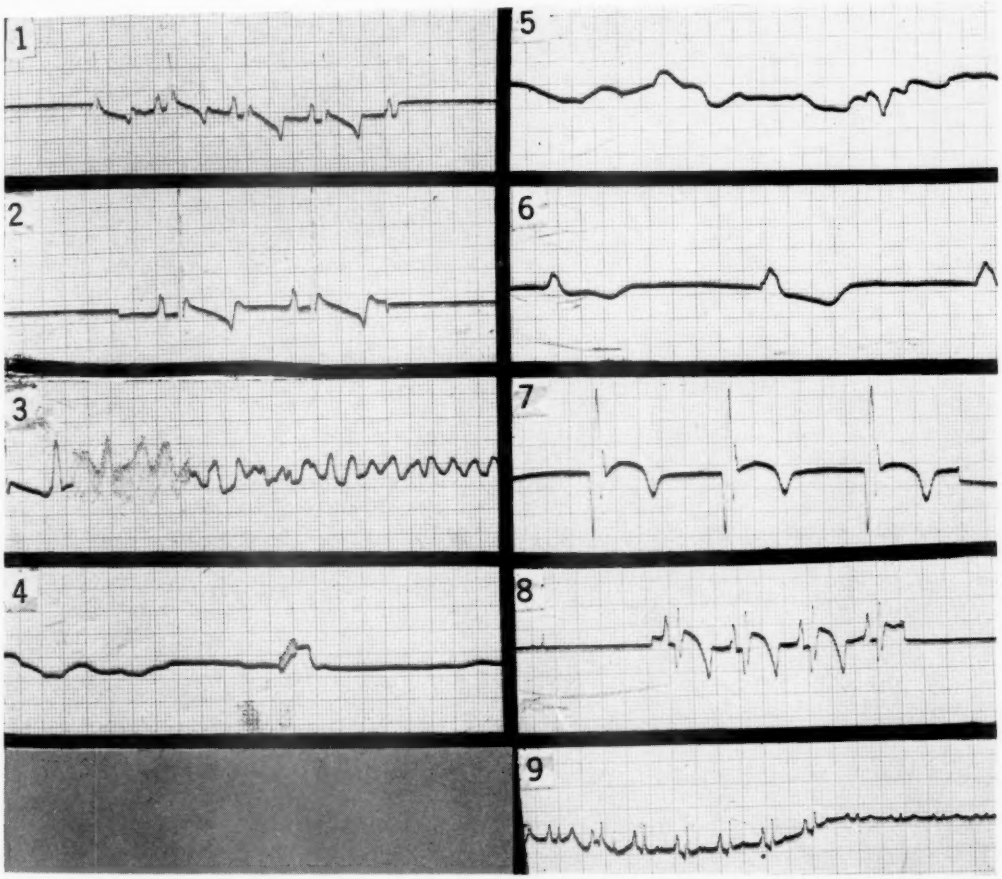

Fig. 2.—Serial electrocardiograms (Lead II), Dog No. 15, during electrolyte defibrillation under hypothermia, temperature 23° C. *1*, Normal sinus rhythm beginning refrigeration, temperature 28° C.; *2*, Lead II immediately before fibrillation, temperature 23° C.; *3*, fibrillation by electrical stimulus; *4*, defibrillation by potassium choride; *5*, re-establishment of electrical activity after injection of sodium lactate; *6*, coordinated beat following Ringer's lactate; *7*, beginning the rewarming period, sustained beat, temperature 24° C.; 8, regular sinus rhythm at 28° C.; and *9*, electrocardiogram the following day.

Encouraged by the results of controlling ventricular fibrillation and with a technique for effective cardiac resuscitation, the authors decided to employ the hypothermia technique for a direct approach on the left atrium and ventricle. In a series of 7 dogs, therefore, left atriotomy or ventriculotomy

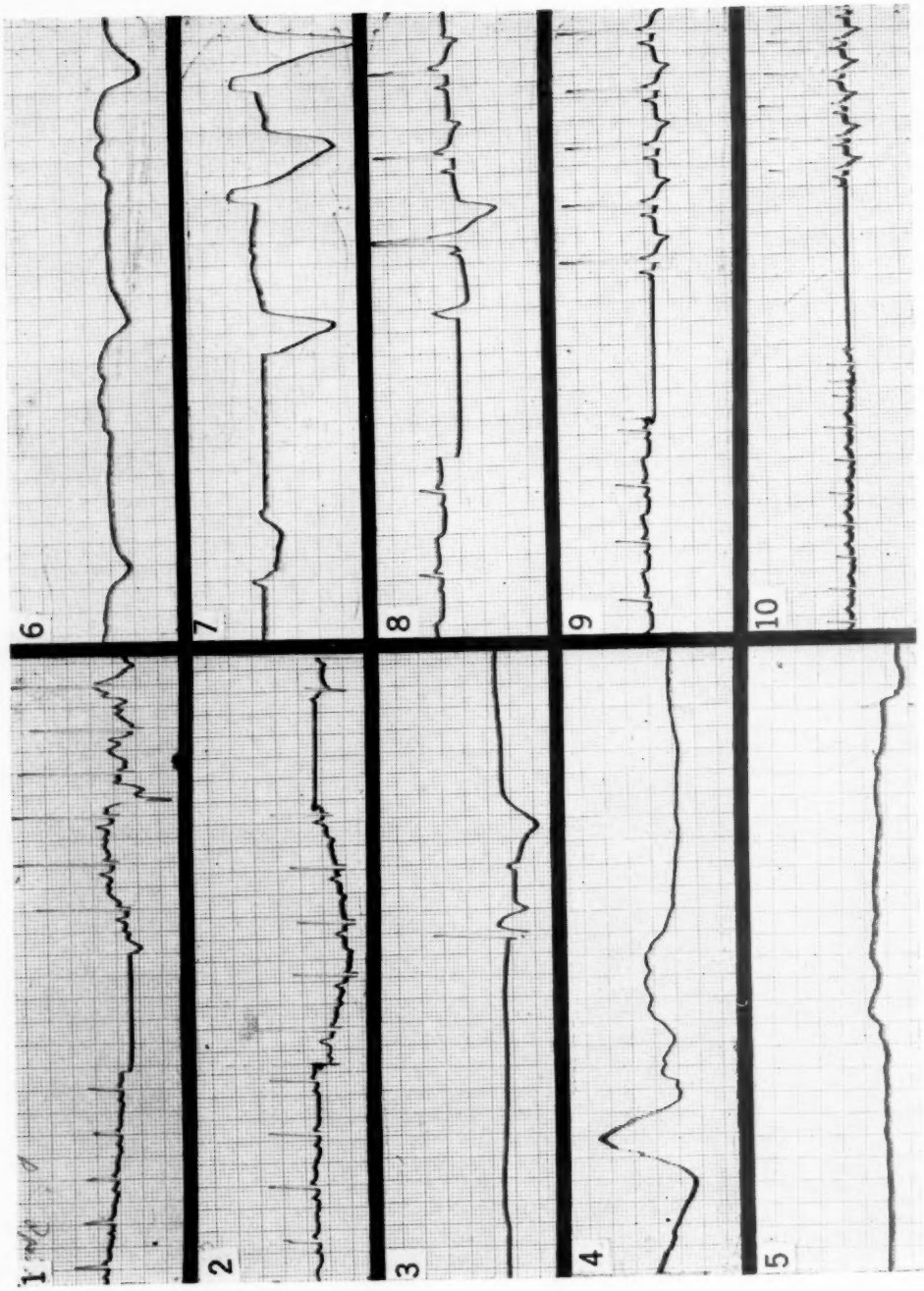

Fig. 3.—Serial electrocardiograms (Leads I and II), Dog No. 40, during and after right ventriculotomy at 19° C. *1*, Normal sinus rhythm before refrigeration, temperature 34° C.; *2*, recording of Leads I and II at 28° C.; *3*, Lead II immediately before ventriculotomy, temperature 19° C.; *4*, defibrillation with potassium chloride; *5*, re-establishment of electrical activity after 15 min. cardiac standstill including right ventriculotomy of 8 min duration by injection of molar sodium lactate, temperature 19° C.; *6*, coordinated beat 1 min. after Ringer's lactate; *7*, Leads I and II beginning the rewarming period, temperature 21° C.; *8*, regular sinus rhythm, 25° C.; *9*, Leads I and II, 30° C.; and *10*, recording of Leads I and II on following day.

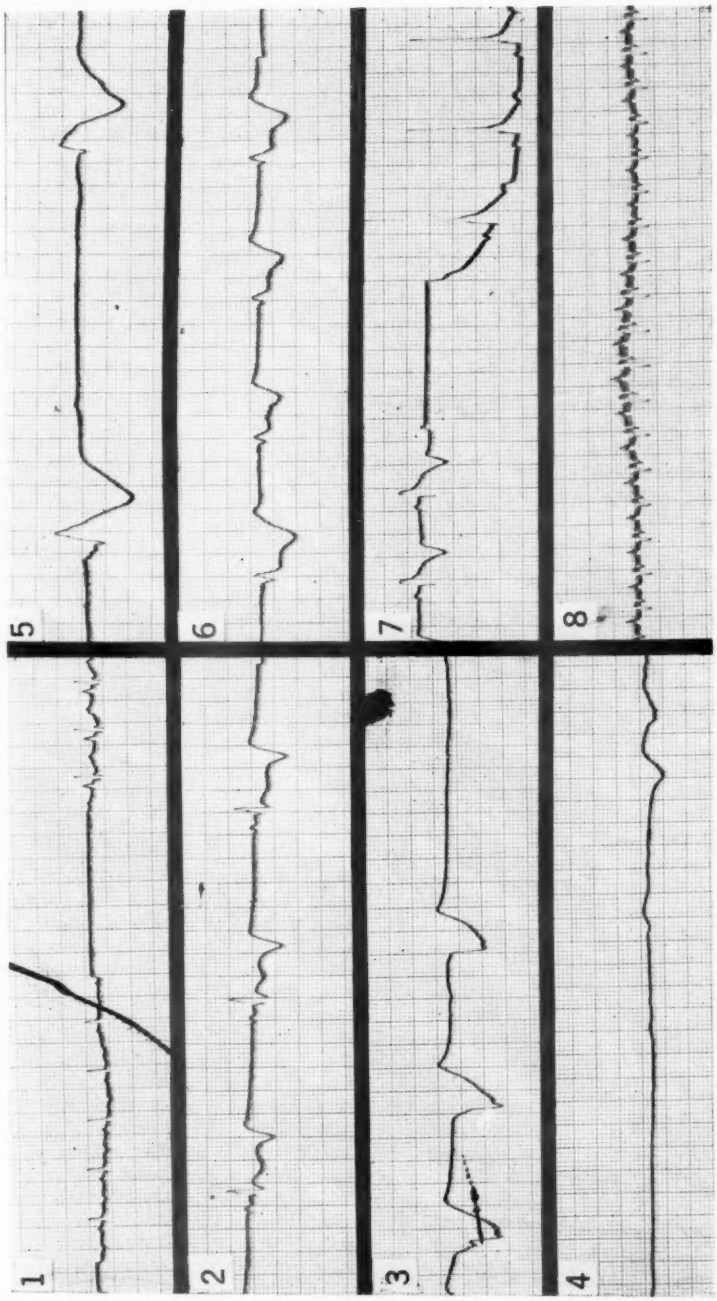

Fig. 4.—Serial electrocardiograms (Leads I and II) obtained at 21° C. during left atriotomy on Dog No. 34. *1*, Normal sinus rhythm beginning refrigeration, temperature 35° C.; *2*, Lead II at 23° C. after removal from ice bath; *3*, elective cardiac arrest with potassium chloride at 21° C.; *4*, re-establishment of electrical activity by priming with sodium lactate after 15 min. cardiac standstill (left atriotomy 8 min. duration); *5*, coordinated beat after injection of Ringer's lactate; *6*, sustained beat during the rewarming period of 23° C.; *7*, Leads I and II showing regular sinus rhythm at 25° C.; and *8*, recording of Lead II on following day.

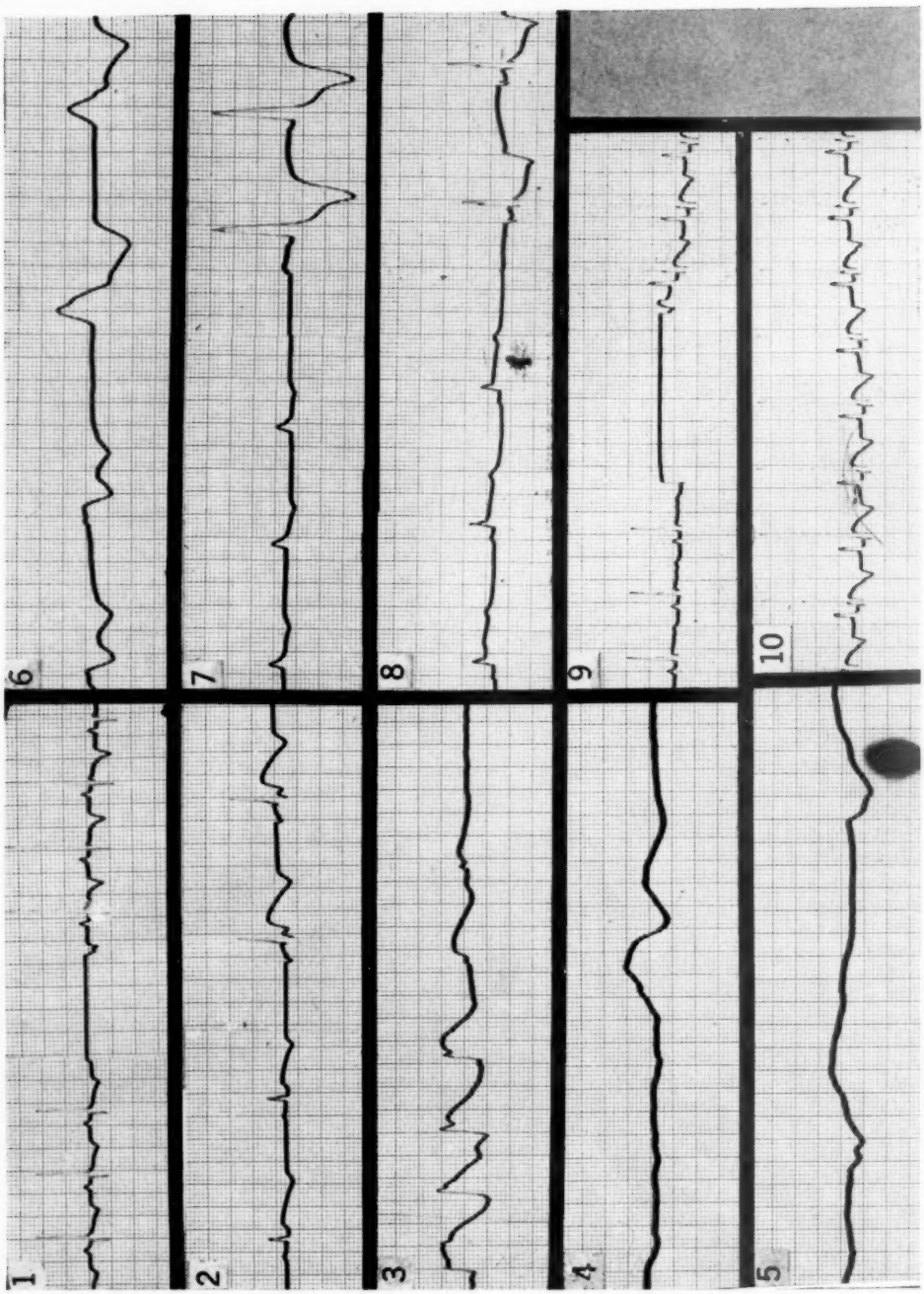

Fig. 5.—Serial electrocardiograms (Leads I and II) obtained at 24° C. during left ventriculotomy on Dog No. 37. *1*, Normal sinus rhythm beginning refrigeration, temperature 34° C.; *2*, Leads I and II on removal from ice bath at 25° C.; *3*, elective cardiac arrest with potassium chloride at 24° C.; *4*, re-establishment of electrical activity by injection of sodium lactate after 12 min. of cardiac standstill (left ventriculotomy of 8 min. duration); *5*, coordinated beat after Ringer's lactate; *6*, Leads I and II at 24° C. after beginning rewarming period; *7*, Leads I and II at 25° C.; *8*, regular sinus rhythm on Leads I and II at 26° C.; *9*, Leads I and II at 30° C.; and *10*, postoperative recording 8 hours after rewarming.

was done under elective cardiac arrest induced by potassium chloride. Wide exposure of the mitral valve was possible in a bloodless field for periods of 5 to 8 minutes. The original method has been modified to include aortic injections and the following technique has been established. In large mongrel dogs, cooled to temperatures from 21° to 25° C., 3 c.c. of potassium chloride diluted with 10 c.c. of arterial blood aspirated into a heparinized syringe was injected into the proximal ascending aorta occluded distally. Cardiac arrest usually resulted within 30 seconds. The left atrium or ventricle was incised and the mitral valve was exposed and manipulated. Either cardiac chamber was then closed after proper air displacement, using Ringer's solution. Resuscitation was started by releasing the venous inflow and by applying gentle cardiac massage to clear potassium chloride from the coronary system. After the muscle was well oxygenated, 3 c.c. of sodium lactate was injected into the left ventricle or ascending aorta. The ventricular route was preferred because of its simplicity and accessibility, whereas injection of drugs into the aorta requires good exposure and is done with difficulty through a left thoracotomy incision.

After electrical activity was established, 3 c.c. of Ringer's lactate was given and cardiac massage was continued until a sustained beat resulted. Air embolus was present in one instance and was driven through the coronary system by continuous massage. Survival rate for this series was 100 per cent. Four animals fibrillated initially during cardiac resuscitation but were readily defibrillated with additional doses of potassium chloride.

RESULTS

Defibrillation.—Forty dogs were fibrillated by electrical shock in 46 instances. In all animals ventricular fibrillation was stopped by 2 to 3 c.c. of 15 per cent potassium chloride injected into the left ventricle. The average time for successful defibrillation was 10 seconds. Five animals were converted to rhythmic beats spontaneously after potassium injection.

Resuscitation.—All 47 dogs in a 15° to 29° C. temperature range were resuscitated from cardiac standstill with intracardiac injection of 3 to 4 c.c. of sodium lactate followed by equal amounts of Ringer's lactate combined with cardiac massage. The largest number of experiments were performed between 19° and 24° C.

Elective Cardiac Arrest for Intracardiac Surgery.—Seven dogs have been subjected to left atriotomy and/or ventriculotomy at temperatures ranging from 21° to 25° C. with exposure of the mitral valve for 5 to 8 minutes. The average time for cardiac arrest was 10 minutes. All animals survived the procedure.

DISCUSSION

Knowledge of the various cations on cardiac rate and rhythm has existed since Ringer's[10-12] basic investigative work in 1882-1883. Later D'Halluin[4] in 1904 and Hooker[6] in 1929 used potassium chloride to stop ventricular fibrillation. In order to restart the heart, D'Halluin used Lock's solution while Hooker

recommended a solution of calcium chloride and adrenalin. Swan and associates used potassium chloride to reverse fibrillation in hypothermia. More recently Bellet, Wasserman, and Brody[1, 2] drew attention to the effect of sodium lactate in cardiac arrest, ventricular standstill during Stokes-Adams seizures, atrioventricular heartblock, and sinus bradycardia. In England, Melrose, Dreyer, Bentall, and Baker[8] advocated elective cardiac arrest with potassium citrate as an aid in heart surgery. In this country the Melrose technique has been successfully used on patients by Effler,[5] Kolff,[7] and their associates.

The results of our experiments confirm the findings of other investigators; that potassium can be successfully used to elicit elective cardiac arrest and to convert ventricular fibrillation to cardiac standstill. The experiments suggest the use of sodium lactate and Ringer's lactate combined with cardiac massage as a valuable aid in cardiac resuscitation during hypothermia.

The mechanism of the observed cardiac effects of sodium, potassium, and calcium are not entirely established, and at low temperatures little is known of the underlying physical or chemical changes through which these elements influence the heartbeat. Cold, as well as calcium, decreases permeability of the cell membrane; potassium, on the other hand, increases cell membrane permeability. Perhaps the excitability of the muscle fiber is dependent upon the concentration of H ions on each side of the cell membrane. Calcium and potassium, by alternating cell membrane permeability, may effect diffusion of H ions and vary their concentration. As a result a difference in electrical potentials is produced. The action of sodium is not clear but many observations have shown that the increased sodium content of the extracellular fluid increases intracellular conductivity. In Figs. 2, 3, 4, and 5, increased electrical activity can be noted immediately after the injection of sodium lactate. In addition the alkalosis caused by sodium lactate and Ringer's lactate accelerates the heart rate by facilitating conductivity. Ringer, in his original work, noted that when in the isolated perfused heart the ventricles lost their contractility this could again be restored by sodium bicarbonate solution. Perhaps sodium bicarbonate acts by its alkalinity. Similarly Mines,[9] in 1912, had shown that electrical and mechanical excitation decreased with acid pH.

In considering the lactate, Bing[3] showed evidence that the heart muscle can utilize this substance for direct combustion. The lactate may act as added substrata to Krebs's cycle and therefore be converted to pyruvate by diphosphopyridine nucleotide.

SUMMARY

In 47 dogs under hypothermia, ventricular fibrillation, cardiac arrest, and resuscitation were successfully accomplished by using various solutions of potassium chloride, sodium lactate, and Ringer's lactate. Although further investigation should be done, this technique may offer an opportunity for useful surgery in the motionless heart, without the danger of air embolism.

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(End of Society for Vascular Surgery papers.)

THE UTILIZATION OF VINYLITE PLASTIC CASTS TO DEMONSTRATE CORONARY AND INTERCORONARY ANASTOMOTIC VESSELS

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THE purpose of the present investigation is to study methods of revascularization of the myocardium by diverse means, utilizing an injection dye technique in an attempt to demonstrate in an objective manner the nature and extent of new sources of blood supply to the myocardium. The matter of these observations will be presented in a future publication. This preliminary report concerns a simple, inexpensive, and eminently satisfactory technique for the post-mortem visualization of coronary and intercoronary vessels. The technique offers a complete tridimensional injection cast of the arterial and venous system including the precapillary arterioles and venules. Moreover, the finer divisions of the coronary arteries present a far more complex picture than the larger vessels, the knowledge of which is still incomplete and in some cases controversial.[10] It is in such cases that the medium suggested herein has been found to penetrate consistently the most minute arterioles, in instances as fine as 0.03 mm. in diameter, with the production after corrosion of a nonfriable, nonbrittle multicolored cast of the entire coronary circulation, including the deeply penetrating myocardial branches.

The literature discloses innumerable anatomical investigations both in man and in animals for investigating the vascular systems of the human body. In these investigations, dyes have always occupied a principal place, and colored fluids, water, inks, and stains have supplemented simple dissection. Of more modern techniques, those reviewed in the monographs of Spalteholz,[7] Gross,[3] and Whitten[11] culminated in the significant contribution of Schlesinger,[6] who devised a technique of unrolling the heart so that the arterial system could be examined in one plane. These and other discussions over many decades have been provoked because of their direct clinical implications in the evaluation and comprehension of angina pectoris, myocardial infarction, and other pathologic conditions of the human heart, particularly those in which relative cardiac anoxia is present.[1, 2, 5]

The medium used in the Schlesinger technique consists of a radiopaque lead-agar mass injected into the coronary arteries with subsequent visualization in one plane. Such a medium, however, while possessing the great merit

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that it does not pass through the capillary bed in normal hearts, has the disadvantage that a great deal of time is necessary in preparation of the medium; moreover, it is frequently found after preparation to be unstable. Furthermore the mass rarely fills the most minute arterioles, and the apparatus required is more detailed than that reported here. The drawbacks of the Schlesinger method are that the heart is visualizable in one plane only, and inevitably in the unrolling dissection technique many coronary artery branches are severed.

In 1950, Kazzaz and Shanklin[4] first demonstrated the normal coronary anatomy of the dog using colored plastic (vinyl acetate) injections and corrosion. Stern[8] in 1954 used the method to demonstrate the septal artery, and he pointed out that anastomoses could be demonstrated in an unambiguous manner. Modifications of method have been made in the present investigations and vinylite plastic casts have been utilized to demonstrate the presence of coronary and intercoronary anastomotic vessels.

THE PRESENT STUDY

Fifty canine hearts from animals weighing between 15 and 150 pounds have been injected, with comparative studies in human, bovine, porcine, feline, and simian specimens. In all cases, both coronary arteries and the venous coronary system have been injected, and careful studies of arterial variations and communications have been made. In addition, the technique has been used to examine the action of various drugs upon the coronary circulation, particularly Adrenaline, papaverine, and iodoacetic acid. Several demonstrations of intercoronary anastomotic vessels have been prepared, showing absolute demarcation of different-colored dyes, in sharp contrast to the somewhat fused admixture of colors obtained by other methods.

TECHNIQUE

Apparatus.—The apparatus consists of a simple manometric gauge as used on a sphygmomanometer. This is supported by means of a common clamp, and is connected via a T piece glass conduit to a 25 c.c. Luer Lok all-glass syringe with a metal locking adapter. Mayon tubing is used for connecting the arms of the T piece with the gauge and with the syringe, respectively. The size of the syringes depend upon the size of the heart to be injected, a 10 c.c. syringe being very satisfactory for a cat's heart, while a 25 c.c. syringe is required for a bovine heart.

The injection needles are blunt-nosed cannulae varying from 12 to 25 gauge. These needles are made of rust-resistant steel, and are of varying lengths, the ease of injection being frequently dictated by the dimensions of a particular needle under a given circumstance.

Simple hemostats, 00 silk, and fine and heavy surgical scissors complete the equipment necessary. The medium employed is vinyl acetate, a commercial product known as Vinylite.* Vinylite is a plastic dissolved in acetone and is

*Vinyl acetate is obtainable in all three colors from Ward's Natural Science Establishment, Box 24, Beechwood Station, Rochester, N. Y.

sold in a 12 per cent solution. It is procured in three colors—red, blue, and yellow. It has been customary in our studies to inject the right coronary artery with yellow plastic, the left coronary artery with red plastic, and the coronary venous system with blue plastic. If the containers are kept sealed from the air, the dye may be stored indefinitely, although it is mandatory to shake it well before use on every occasion to ensure a thorough mixing of the color.

One precaution must be emphasized. The rapidity with which the plastic sets upon contact with water requires that all instruments be scrupulously dry.

To prevent clotting of needles and the jamming of syringes, these are kept at all times in acetone, and, prior to any injection, the syringe and needle are washed thoroughly with acetone solution.

METHOD OF INJECTING THE CORONARY ARTERIES

The coronary arteries are injected immediately after death. The heart should be as fresh as possible. Hearts have been injected within ten minutes of death, and others after they have been frozen for several days. It is our general impression that the injection is more complete and slightly less pressure is required with immediate preparation, although we have not noted any consistent difference or untoward variation in those hearts which have been frozen, save that time is needed for the heart to defrost and to return to room temperature.

It has never been found necessary to relax the vessels by perfusing them with a solution of potassium sulfocyanide as suggested by Gross,[3] or with physiologic saline solution. Routinely, within seconds of its removal from the cadaver, all blood clots from the heart are thoroughly washed away in warm running water.

The right and left coronary arteries are then dissected free as they originate from the aorta and the blunt-headed cannulae are securely fastened into them as close to the origin of the vessels as possible with 00 silk sutures. Use of a bowknot facilitates removal of the cannulae after injection has been completed. Heavy artery clamps are affixed from the outside around both the vessel and the cannulae to hold them secure. In the case of the left coronary artery, the anterior descending branch and the circumflex branch are cannulated and injected separately with a different-colored dye, if so desired. Cotton gauze plugs are packed into the pulmonary artery and into the aorta at the level of the semilunar valves in order to prevent reflux of the injection mass into the ventricular cavities.

The vinyl acetate is then drawn into a syringe (Luer Lok) previously rinsed with acetate and injected. The pressure applied is intermittent but has seldom exceeded 140 mm. Hg, and frequently has been found to be much less. By a similar routine, the remaining coronary artery may be injected with a contrasting-colored dye. The cannulation of the coronary sinus is achieved by making an incision in the right auricular appendage, identifying the mouth of the sinus and that of the middle cardiac vein, and plugging the atrial and

ventricular cavities with gauze as before. The injection procedure is repeated as described. At the completion of the injection process, all plugs are removed from the ventricular cavity and from the pulmonary artery and aorta and the chambers of the heart are inspected for any leakage of dye that might have flowed back.

Throughout this procedure the heart, unlike several alternate techniques, is not suspended in any form of fluid and lies free on the work tray. The injection is completed in from 10 to 15 minutes depending on the size of the heart. The pressure is maintained in the vessels after injection by permitting the heavy clamps to remain about the cannulae for several seconds, but the remarkable properties of the plastic preclude any shifting of the mass soon after injection.

The cannulae are then removed and the injected specimen is allowed to harden for several hours, usually overnight. During this time, there is some slight contracture and diminution in the size of the injected vessels. The final corrosion cast is then prepared by macerating the myocardium and pericardial adipose tissue in 10 per cent potassium hydroxide for twenty-four hours. The specimen is submerged in a pan of alkali at room temperature. The following day, the cast is rinsed gently under a fine spray of running water, immersed momentarily in sodium hypochlorite bleach to remove any remaining tissue, and mounted finally either dry or in water.

Where intercoronary anastomoses are found, use of several colored plastics shows a sharp and readily identifiable demarcation. Such preparations allow also the study of the finest details of the coronary circulation.

Should for various reasons the myocardium be required for study, radiopaque vinyl plastic may be made by adding iodoform to the plastic, using one part of iodoform to nine parts of plastic.[9] This does not change the properties of the plastic but renders it opaque to x-rays. By this method, preparations as described by Gross or those of Schlesinger using his unrolling and dissection procedure may be made.

In all cases, however, the plastic corrosion preparation is preferred since it is simply planned and executed, permitting visual demonstration in a superior manner of the finer arteriolar branches that other available techniques fail to demonstrate. This difference is particularly well presented in the auricular cast. Moreover, the system is viewed as a three-dimensional model and eliminates the confusion of the overlapping of arterial shadows as in the Gross technique and is in marked contrast to the flat projection viewed by the Schlesinger method.

ILLUSTRATIVE CASES

Only six of the many injected specimens are selected to illustrate the possibilities in a study of intercoronary communications.

Demonstration I (Fig. 1).—This cast presents a normal canine heart with both coronary arteries and the coronary venous system (other than the Thebesian channels) injected.

Demonstration II (Fig. 2).—Dog 698. A 20 kilogram dog under Nembutal anesthesia was operated upon on April 6, 1956. The heart was exposed through an intercostal incision. The pericardium was opened, and the circumflex branch of the left coronary artery was ligated. The animal recovered and was returned for reoperation on Aug. 3, 1956, after a period of four months. The chest was reopened and the anterior descending branch of the left coronary artery was ligated. The heart immediately fibrillated and the animal succumbed. The injection study as demonstrated below revealed quite clearly: (a) a definitely established communicating intercoronary anastomosis between the right and left coronary artery; (b) retrograde filling of the circumflex branch of the left coronary artery distal to the point of previous occlusion. This had been made possible by the anastomoses of branches from the anterior descending branch of the left coronary artery uniting with branches from the circumflex vessel in the region of the apex of the heart.

Demonstration III (Fig. 3).—Dog 777. An 18 kilogram dog under Nembutal anesthesia was operated upon on March 21, 1956. The heart was exposed through a sternal incision. The pericardium was opened. Utilizing a segment of the mid stomach, an overlay gastrocardiopexy was performed after excision of the mucosa. The circumflex branch of the left coronary artery was dissected from its bed near the origin and a ligature passed under it, the lumen then being completely occluded by tying the ligature firmly.

The animal recovered and was reoperated upon on Aug. 6, 1956 (four and one-half months later). The remaining major branch, the anterior descending of the left coronary artery, was dissected free from its bed at its origin, a ligature passed under it and the vessel completely occluded.

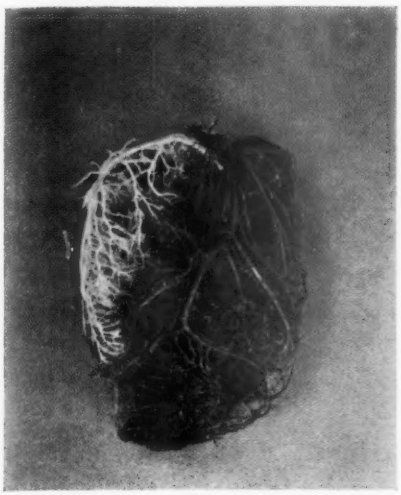
The animal survived this procedure for five hours (both branches of the left coronary artery having been now occluded) before it was sacrificed. The injected cast is visualized in the figure where three major intercoronary anastomotic bridges between branches from the right and from the left coronary artery are clearly defined. The distribution of the right coronary artery shows also an unusual and increased area of supply.

It is noted that no passage of dye was observed to pass between the coronary vessels and any vessels of the overlay gastrocardiopexy. *It is probable that the intercoronary anastomotic vessels were provoked by the acute ligation.*

Demonstration IV (Fig. 4).—In this demonstration, 4 c.c. of 1:1,000 Adrenaline was instilled into the left ventricle a few moments before sacrifice. Injection of the heart was immediate. The immense response of the coronary vessels is clearly seen, particularly the fine brushlike vessels that penetrate the thick myocardial muscle.

Demonstration V (Fig. 5).—The septal coronary artery is a branch of the left coronary artery. This artery constitutes the major coronary supply to the interventricular septum, and as Donald and Essex have shown, has a very variable site of origin. The technique described herein has been found of constant use in demonstrating this important vessel, and the visualization so obtained has been superior in our hands to those obtained by other methods we have tried.

Fig. 1.



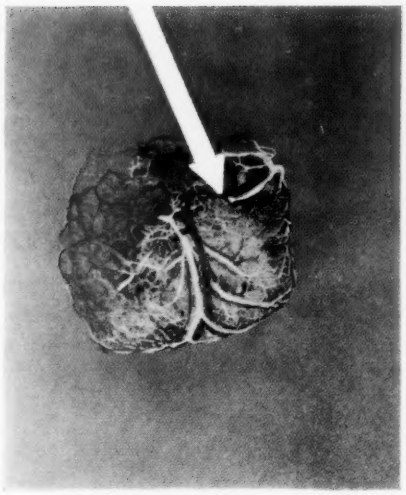
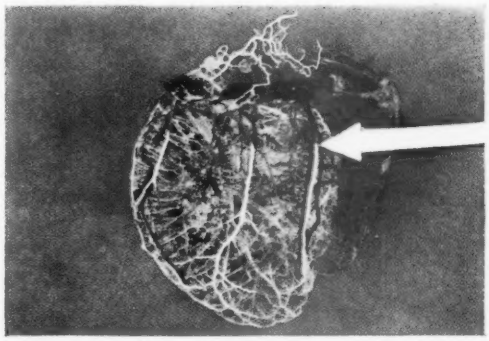


Fig. 2.

Fig. 3.



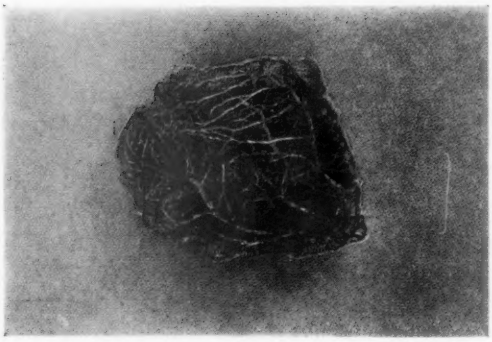
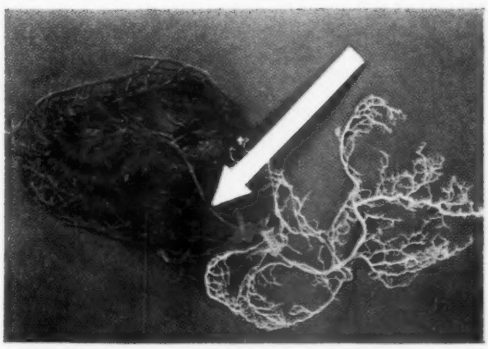


Fig. 4.

Fig. 5.



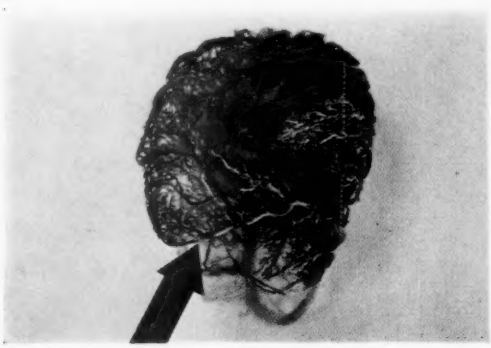


Fig. 6.

Fig. 1.—Vinyl plastic cast of normal dog heart. Right coronary artery—yellow; left coronary artery—red; coronary venous system—blue

Fig. 2.—Circumflex artery filled with yellow plastic distal to point of ligation (arrow) thus demonstrating retrograde filling via anastomoses between the anterior descending and circumflex branches of the left coronary artery. Canine heart.

Fig. 3.—The arrow points to an intercoronary anastomosis. Two similar anastomoses are seen at the same level in the other main branches. A total of four intercoronary anastomoses can be clearly seen in this figure. Canine heart after cardiogastropexy followed by acute ligation of residual branch of left coronary artery.

Fig. 4.—Injection cast immediately after instillation of Adrenaline into the left ventricle. Canine heart.

Fig. 5.—Normal dog heart. The septal artery (arrow). The right coronary artery (yellow) has been displaced outward.

Fig. 6.—Vinyl plastic cast of a human heart. The arrow points to a clearly defined intercoronary anastomosis at the apex of the heart. The apex is tilted toward the camera.

Demonstration VI. Human Cast (Fig. 6).—A 28-year-old white married (para v) woman was admitted first to the Neurosurgical Service on Feb. 18, 1956. She complained then of symptoms which she had had since October, 1955. At that time she was pregnant. She developed diplopia in January, 1956. This continued and her gait became staggering. She complained of headache, nausea, and vomiting and became unable to stand because of loss of balance. Six weeks prior to admission personality change had occurred.

The clinical diagnosis of a possible pineal tumor was made. She received cobalt therapy and upon completion of this was discharged in an improved condition. She was subsequently readmitted on Sept. 2, 1956. She took a gradually downhill course, became moribund, and expired on Oct. 3, 1956.

Autopsy revealed a tumor in the region of the third ventricle. There were no signs of cardiac or pulmonary pathology other than a terminal pneumonia.

COMMENT

There was at no time in this patient's history any knowledge of rheumatic or other cardiac illness. There had never been any pulmonary illness or limitation. She had no history of severe or chronic anemia noted. She had never had a thoracotomy or any cardiac procedure. The injection cast of her coronary vascular system revealed a grossly normal anatomy. There were few contortions of the principal arteries speaking against the arteriosclerotic changes very evident in the injection casts of older individuals. In the region of the apex of the heart a union of two distinctly different-colored dyes had occurred, revealing a patent passageway between the right and left coronary arteries mediated through a minor branch between the anterior descending branch of the left coronary artery and a branch from the posterior descending branch of the right coronary artery. The cast is visualized in Fig. 6.

SUMMARY

1. Fifty canine hearts, and several human, bovine, feline, and simian specimens have been injected by the above technique to demonstrate coronary and intercoronary anastomotic vessels at post mortem. The method also has yielded superior demonstrations of the septal coronary artery.

2. The technique is rapid, complete, simple, and economical, and a tridimensional cast is visualized.

3. The injection mass is a commercially available product, rapidly injectable and hardens almost simultaneously.

4. Vessels down to the size of 0.03 mm. are easily visualizable, and the distribution of the multicolored masses in the coronary artery branches gives an absolute index of the distribution of the blood from either coronary artery orifice.

5. This injection dye technique is being utilized in an attempt to demonstrate in an objective manner the nature and extent of new sources of blood to the myocardium following revascularization procedures. The matter of these observations will be presented in a future publication.

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SURGERY UNDER DIRECT VISION FOR THE CORRECTION OF PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM

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CONGENITAL pulmonary stenosis with intact ventricular septum has been considered a rare disease. Since the development of newer techniques for the correction of this defect, however, the number of cases reported in the literature has increased surprisingly.

Sellors[19] and Brock[5] described in 1948 a technique for blind transventricular pulmonary valvulotomy and infundibulectomy which has been widely accepted all over the world as a valuable procedure, and a great number of reports showing the results of Brock's technique for the relief of "pure" pulmonic stenosis have appeared in the literature.

The clinical reports are very encouraging, showing marked improvement of the patient's condition. The postoperative catheterization findings, however, have been very disappointing[3, 4, 11, 12, 14, 18] revealing that the obstacle to the pulmonary circulation has not been completely removed. Since there remains a high pressure in the right ventricle, it is probable that the patient may have trouble in the future because of the partial obstruction which is not yet completely relieved. Considering that a patient may have pressure of above 200 mm. Hg in the right ventricle with no symptoms whatsoever, our judgment of the case must be obtained from catheterization findings. This is the only way to get a more definite idea of the hemodynamic changes. Therefore clinical judgment only cannot give us any objective data about the real improvement of the physiologic condition of the patient after operation.

The ideal technique should correct the stenosis with the disappearance of the pressure gradient without producing valvular insufficiency. It is evident that this might be possible only when a technique which permits the opening of the stenotic valve under direct vision is used. Swan and associates,[4] using hypothermia, were able to open the pulmonary artery and cut the pulmonic valve under direct vision. Later on, they proved that there was no gradient of pressure between the right ventricle and pulmonary artery. Although the employment of hypothermia by Swan and co-workers has been relatively a safe procedure, in our laboratory[10] the use of hypothermia was very discouraging because of the high incidence of ventricular fibrillation. Moreover, this procedure

A preliminary report about this subject was read before "Associação Paulista de Medicina," Nov. 16, 1955.

The pressure tracings were obtained in the Hemodynamic Laboratory of the Anita Pastore D'Angelo Foundation, under the direction of Adauto Barbosa Lima, M.D.

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would not permit correcting "pure" infundibular stenosis, since the risk of ventricular fibrillation is still higher when ventriculotomy is done. This has been a common experience in several other centers as well.

The experiments of Andreasen and Watson[1] and Cohen and associates,[6] demonstrating that dogs receiving blood from their azygos vein after occlusion of venae cavae could be maintained for a long period without any discernible ill effect to the body being shown, opened a new road to the coardiac surgery. Lillehei, using the azygos flow experimental studies as a basis, was able to perform the total by-pass of the heart of patients either by the method of controlled cross circulation or by continuous arterial perfusion from a reservoir of arterialized venous blood. The obvious disadvantage of using a healthy donor stimulated us to develop a new way to solve the problem of surgery under direct vision for the correction of defects on the right side of the heart.

In 1955 we worked out a new procedure which allows direct vision of the pulmonary valve or the right ventricular cavity with safety and without the complexities of the other techniques used up to the present date.

This new procedure was based on the azygos flow principle, which allowed the by-pass of the right side of the heart by using a Sigmamotor pump machine to replace the right ventricle, while the lungs and the left side continued to work normally, the blood being oxygenated by the patient's lungs. The results were most gratifying and the new technique was duly employed on two patients. This will be the subject of another article. The present paper will describe the results of our experimental work.

EXPERIMENTAL METHOD

The method was employed in 42 mongrel dogs, completely unselected as to size, age, and sex. The anesthesia was obtained with the intravenous injection of 0.04 mg. Nembutal per kilogram of body weight. The animals were intubated with a cuffed endotracheal tube and the respiration was maintained mechanically with continuous administration of oxygen.

The heart and lungs were exposed through an anterior transverse incision at the level of the third or fourth intercostal space. The sternum was transected and both sides were incised. The pericardium was opened. Both venae cavae were dissected up and the azygos vein ligated 2 cm. distal to its junction with the superior vena cava. A piece of umbilical tape was then looped around each vena cava and both free ends were threaded through a rubber tubing. By pulling up on the tapes and slipping the rubber tube down against the venae cavae it was possible to occlude both veins. A No. 12 Fr. catheter was introduced into the superior vena cava through the proximal end of the azygos vein and another catheter was introduced into the inferior vena cava passing through the right auricular appendage. The catheters were previously filled up with heparinized saline solution. The inferior or medium pulmonary branch of the right pulmonary artery was dissected and a No. 12 Fr. catheter was introduced in this vessel with the extremity pointing toward the pulmonary trunk. Both lungs continued to receive blood except for the lobe corresponding to the cannulated branch.

After cannulization of both the venae cavae and the branch of the right pulmonary artery in its distal part, the pump was set up and the tubes were filled with heparinized saline solution. The pump was previously calibrated in order to deliver an output of 20, 30, or 45 c.c. per kilogram of body weight per minute. These figures correspond to approximately two, three, and four times the azygos flow. The total dose of anticoagulant used was 1 mg. of heparin per kilogram of body weight diluted in the saline used to fill up the catheters and plastic tubes of the extracorporeal circuit.

After the pump was turned on, both venae cavae were occluded around the catheters previously inserted, and the extracorporeal circulation was maintained during 30 minutes in each experiment. This procedure was used to visualize: (1) the pulmonary valve through an opening in the pulmonary artery; (2) the right ventricular cavity by transventricular incision; and (3) the right auricular cavity by direct auriculotomy.

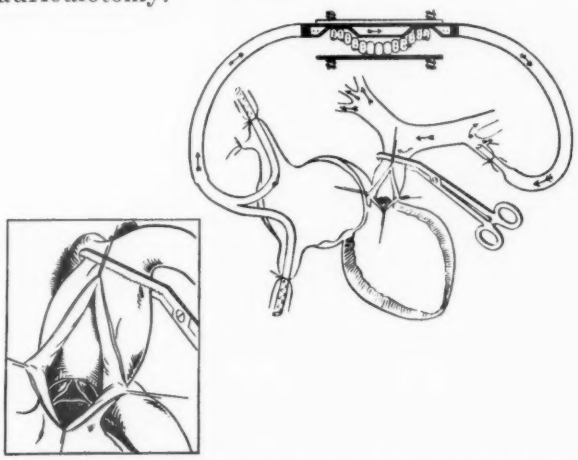

Fig. 1.—The pulmonary valves exposed by an opening through the pulmonary artery during the by-pass of the right heart.

Through an incision in their walls both the right ventricle and the pulmonary artery were exposed simultaneously, in some experiments. The coronary sinus blood was aspirated continuously and it was not necessary to reinfuse this blood in any case. The visualization of the pulmonary valve and the auricular and ventricular cavities was perfect.

The opening of the main pulmonary artery (Fig. 1) was done by a longitudinal incision in its anterior wall. This artery had been clamped previously with a curved Potts clamp, which pinched off a small lateral segment of the vessel. Four threads were put along the incision to help the opening of the artery after release of the Potts clamp. Before the Potts clamp was released, the main pulmonary artery was occluded close to its bifurcation.

The closure of the incision was performed by putting back the Potts clamp, releasing the clamp occluding the artery close to its bifurcation, and closing the longitudinal incision with a continuous over-and-over suture (Fig. 2).

Ventriculotomy.—The opening of the right ventricle was done by a large longitudinal incision, care being taken to prevent any damage to the coronary ramifications. A continuous over-and-over suture was used to close the right ventricle (Fig. 3).

Thirty minutes after the beginning of the by-pass the superior and inferior venae cavae were released and then the pump was stopped. The catheter used to intubate the lobular pulmonary artery was taken off and the artery was closed with a continuous over-and-over suture. The circulation to this lobe was re-established. The catheter used for both venae cavae was pulled out and then the right auricular appendage and the azygos vein were ligated.

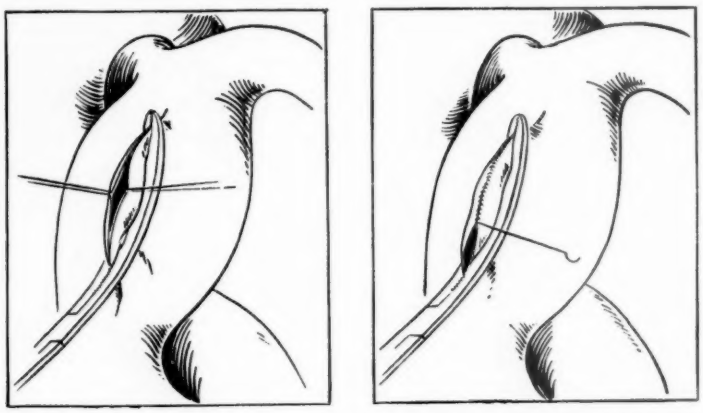

Fig. 2.—Closure of the pulmonary artery incision by continuous sutures over and over.

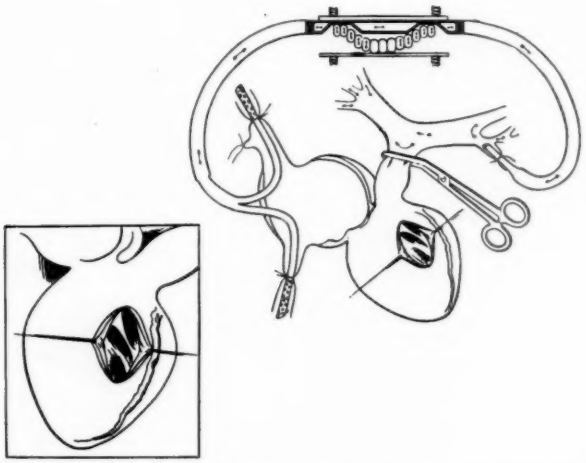

Fig. 3.—Exposure of the right ventricular cavity through a large longitudinal incision on its anterior wall, during the by-pass of the right ventricle.

The pericardium was closed with loose and separated stitches. The pleural cavities were closed after complete re-expansion of the lungs. Penicillin, 1,200,000 I.U., and dihydrostreptomycin, 0.5 Gm., were given during the operation and on the following day.

RESULTS

Forty-two mongrel dogs ranging in weight from 7 to 22 Kg. were used for this investigation. As it can be seen in Table I, three dogs died at the beginning of the by-pass. Two deaths were due to air embolism caused by air introduced through defects in the connections of the tubes. The third death

occurred on account of fibrillation presumably due to large doses of Novocain solution used to fill the catheters (defibrillation was not attempted). One or more operations were performed on the 39 remaining dogs.

In the group of 39 dogs undergoing operation (Table I), there were 9 deaths, all of them unrelated to the by-pass of the right ventricle. Autopsy was done and the causes of death observed were: (1) Four dogs died from hemorrhages through the suture lines in the right ventricular wall a couple of hours after the operation. (2) Four dogs died from large atelectatic zones attributed to an incomplete re-expansion of the lungs before closure of the chest. The chest usually was not drained. (3) One dog had ventricular fibrillation starting as soon as the right ventricle was opened. Defibrillation was not attempted.

TABLE I. OPERATIONS PERFORMED DURING THE BY-PASS OF THE RIGHT VENTRICLE, USING THE AZYGOS FLOW PRINCIPLE

OPERATIONS	NUMBER OF DOGS
Pulmonary arteriotomy	13
Right ventriculotomy	14
Right auriculotomy	2
Right auriculotomy + right ventriculotomy	1
Pulmonary arteriotomy + right ventriculotomy	2
Pulmonary arteriotomy + right ventriculotomy + right auriculotomy	1
Pulmonary arteriotomy + interauricular septal defect	3
Pulmonary arteriotomy + right ventriculotomy + auricular septal defect	3
None	3
Total	42

Each of the surviving dogs was kept under close observation from the immediate postoperative period up to a maximum of 12 weeks. There were no instances of neurologic lesions, blood dyscrasias, or any other complications. After 12 weeks all dogs were killed for the autopsy studies.

COMMENTS

Different outputs were used in order to evaluate the dog's tolerance and the best output to work with, as follows: 20 c.c. per kilogram per minute in 1 dog; 30 c.c. per kilogram per minute in 25 dogs; 45 c.c. per kilogram per minute in 7 dogs. Apparently there was no difference. The dog's tolerance allowed the selection of the output to be used according to the weight of the animal. The smallest output was used only once in the heaviest dog of this series, in order to avoid a very large total output.

Hemolysis test revealed negligible values. Heart rate, pupillary reflex and rectal temperature were registered before, during, and after each operation. The average figures found are shown in Table II.

TABLE II. AVERAGE FIGURES REGISTERED BEFORE, DURING, AND AFTER OPERATION

	BEFORE	DURING	AFTER
Rectal temperature	39°C.	37.1°C.	36.4°C.
Heart rate	144.8	144.7	130
Pupillary reflex	Normal	Normal	Normal

Considering the average values registered there was no modification of the heart rate during the period when the right ventricle was by-passed. A slight decrease was observed after the extracorporeal circulation was stopped. Femoral pulse was regular and of normal amplitude during the experience. There was no change in the pupils at any time.

Thirty minutes after the beginning of the by-pass experiment there was an average 3° C. fall of the rectal temperature. It is important to point out this fall of the temperature when the procedure involves opening of the right ventricle because of the danger of ventricular fibrillation.

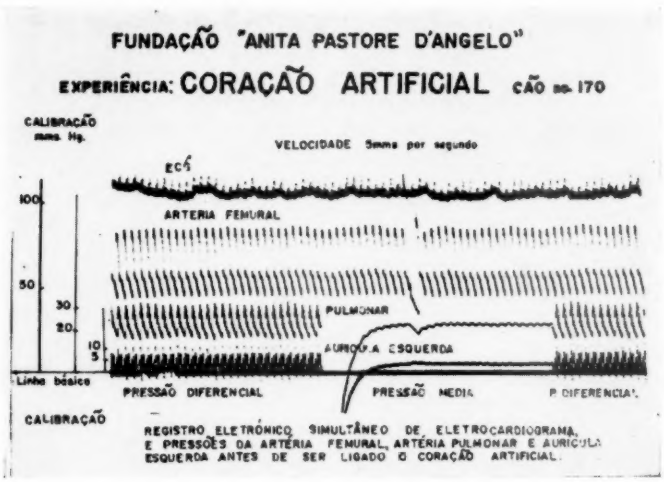

Fig. 4.—Pressure tracings of the pulmonary artery, left auricle, femoral artery, and electrocardiogram simultaneously recorded just before the by-pass of the right heart.

Systemic pressures were measured in the femoral artery during the by-pass of the right ventricle, by intra-arterial technique. In three cases pressure tracings from the pulmonary artery, left auricle, and femoral artery and an electrocardiogram were recorded simultaneously with a Research Recorder* (Figs. 4 and 5).

It was very significant that despite the low output delivered by the machine, the systemic blood pressure remained constant at normal levels, though slightly lower than before the beginning of the experiment. There was no case with definite decrease of the blood pressure, as had been observed during the "cross circulation" technique.

The pulmonary artery pressure was definitely lower during the by-pass, as might be expected on account of the small output. Since in pulmonary stenosis the pulmonary circulation is adjusted to a low pressure and resistance, the fact that the employment of the mechanical pump does not increase the pressure is very encouraging. Further studies with details about pressure changes are being done and will be reported later.

For the prevention of clotting, heparin was the only drug used. The dose was 1 mg. per kilogram of body weight. The total dose was diluted in the saline

*Research Recorder, Electronics for Medicine, New York, N. Y.

used to fill the catheters and plastic tubes which were passed through the pump. Due to the small dose of heparin, it was not necessary to use protamine sulfate in any case. At the end of the experiment the catheters and plastic tubes were checked very carefully and no sign of clot formation could be detected.

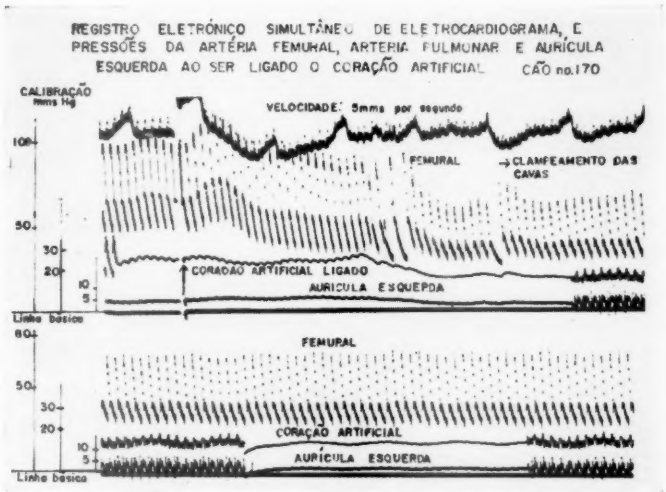

Fig. 5.—Pressure tracings of the pulmonary artery, left auricle, femoral artery, and electrocardiogram simultaneously recorded when the by-pass of the right heart was being initiated. After an initial slight fall the systemic pressure remained constant at the same level.

DISCUSSION

As it was pointed out in this paper, many techniques have been used for the correction of congenital pulmonary stenosis, but judging from the results available in literature, the complete relief of the stenosis was achieved only by Swan[21] who operated upon the pulmonary valve under direct vision, using hypothermia. The disadvantages of hypothermia are well known and this subject has been exhaustively discussed in many recent papers.[2, 7, 13]

Leeds, Puciss, and Siegel[15] and Sewell and Glenn[20] were able to perform experimentally the by-pass of the right ventricle. Dodrill and others[8, 9] employed the by-pass of the right ventricle successfully on one patient for the correction of valvular pulmonic stenosis. Dodrill catheterized the right auricle, and blood from this cavity was pumped into one branch of the pulmonary artery. The total cardiac output was employed. It is difficult, however, to perform this operation smoothly. On the other hand, the suction of blood from the right auricle in patients with pulmonic stenosis is very risky considering that the majority of these lesions are accompanied by an interauricular septal defect or patent foramen ovale.

Lillehei and associates[16, 17] have demonstrated experimentally and clinically that systemic perfusion at reduced rates of flow under normal temperature could be used for totally by-passing the heart and lungs for about thirty minutes, without any discernible ill effects. This has been, so far, the most important contribution to the development of intracardiac surgery under direct vision. However, the application of this principle in cross circulation has the great disadvantage of endangering the life of a normal healthy donor. This has been

overcome by employing a continuous arterial perfusion from a reservoir of arterialized venous blood. Both techniques are very useful when the total by-pass of the heart is necessary. For pulmonic stenosis such a technique would be very laborious and, moreover, the by-pass of the left ventricle is completely unnecessary.

During the past year a new technique for the complete relief of pulmonic stenosis (either infundibular or valvular) without ventricular septal defect was developed in our laboratory. Safety and simplicity were our great aim in developing this new procedure.

The application of the azygos flow principle has simplified a great deal the by-pass of the right heart, allowing the use of a very simple machine like the Sigmamotor pump. Since the rates of flow are about 1/8 or 1/4 of the resting cardiac output for a normal individual of comparable size and weight, the amount of blood by-passed through the pump system is quantitatively small, requiring a very minute dose of anticoagulant. Another advantage is that the blood does not contact a very large surface of tubing so that the destruction of platelets, red blood cells, and fibrinogen is quite negligible. Finally the blood is oxygenated by the patient's own lungs, thus avoiding many complications related to the artificial lung. Considering the simplicity of this new technique in operating under direct vision, it is expected that this will have a large application for the correction of defects on the right side of the heart.

Similar results were obtained in the group of dogs in which large auricular septal defects had been previously made. The success in this group is attributable to the catheterization of the superior and inferior venae cavae instead of the right auricle. The results are very convincing and warrant the application of this technique for the correction of pulmonic stenosis even when there is an associated auricular septal defect.

SUMMARY AND CONCLUSIONS

A new method for the by-pass of the right heart was devised, using a Sigmamotor pump machine and the patient's lung as oxygenator of the blood. It was thus possible to operate upon the pulmonary valve, right ventricular cavity, and right auricular cavity under direct vision.

This new procedure offers the following advantages: (1) From the beginning of the by-pass the right ventricle is completely freed from the stress caused by the stenosis. (2) When the stenosis is valvular, the right ventricle is not hurt since the stenosis is better approached through the pulmonary artery. (3) The pulmonary artery pressure is low during the by-pass, thus avoiding an unnecessary load on the pulmonary artery system which in this condition usually shows a low resistance. (4) Despite the low output used, it was remarkable how the systemic pressure remained constant at slightly decreased levels but still within the limits of normalcy. (5) This technique has been applied without difficulty even when auricular septal defects were experimentally created. (6) This is an excellent method for the correction of infundibular stenosis as well.

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GIANT HYPERTROPHY OF GASTRIC MUCOSA (HYPERTROPHIC GASTRITIS)

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GIANT hypertrophy of gastric mucosa in our experience is not as rare a clinical entity as the literature dealing with this subject would seem to indicate.[3, 5, 6] It assumes importance probably not so much because of its serious aspects as such but because of the difficulty in correctly distinguishing it from gastric malignancy.

This abnormality was first accurately described by Menetrier[9] in 1888 under the term *polyadenomes en nappe*. He divided hypertrophy of the gastric mucosa into two types: *polyadenomes polypeux* and *polyadenomes en nappe;* the former indicating adenomas in the shape of polyps, and, the latter, confluent flat adenomas. The latter term has become synonymous with the term of giant hypertrophy of gastric mucosa.

Many and varied terms have been used to describe this type of gastric hypertrophy, such as giant hypertrophic gastritis, massive hypertrophic gastritis, enlarged gastric rugae, polypoid hyperplastic swelling of the gastric mucous membrane, and adenopapillomatosis gastrica. While the term hypertrophic gastritis is in common use, it is objected to by some pathologists. The reason for this is not clear, unless it is because the lesion is not thought to be primarily inflammatory, or because the term suggests that the lesion is limited to the mucosa when this may not be the case. Being less of a purist in this respect than some pathologists, I will use the term hypertrophic gastritis in this discussion because it seems to fit our clinical needs for the present.

There are various degrees of hypertrophy of the gastric mucosa, and it does not necessarily need to come under the category of "giant" to offer difficulties in differential diagnosis. In the giant type, the stomach, at the time of surgery or when encountered at the autopsy table, has certain distinctive characteristics. The stomach is usually larger than normal, and is not infrequently involved in surrounding adhesions. The adjacent lymph nodes are usually enlarged. The wall of the stomach feels thickened, and the organ, to palpation, gives the feeling of being filled with worms. When the stomach is opened, the mucosa shows a characteristic picture which can best be likened to the appearance of convolutions of the cerebrum (Fig. 7). These tortuous mucosal folds vary from 1 to several centimeters in both width and height. They are found to be freely movable, not being bound down to the surrounding submucosa and other layers of the gastric wall.

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Microscopically, the glandular pattern and cellular components of the mucosa do not show evidence of neoplastic change, and, aside from mild inflammatory reaction and edema, the thickening is largely due to mucosal hypertrophy. The remainder of the gastric wall, while less involved, may show mild inflammation.

The extent of hypertrophy of the gastric mucosa varies greatly. It may be confined to a comparatively small area, or practically the entire gastric mucosa may be hypertrophied, as shown in Fig. 7. It is characteristic that the hypertrophy does not shade off gradually into normal mucosa, but ends abruptly. The condition seems to show a predilection for the mid-third of the stomach with the greater curvature most commonly involved. The antrum, the lesser curvature, and the cardiac end of the stomach have been found to be less frequently the site of involvement.

The condition is more frequently found in males, being reported to be two to three times more common in this sex. In our series it occurred five times as frequently. It occurs most frequently in an age group somewhat younger than that for cancer of the stomach.

The cause of giant hypertrophy of the gastric mucosa has so far not been explained. Nothing in the individual's habits, particularly as related to the ingestion of food, seems to be of significance. The mild inflammatory reaction and edema, particularly as shown in the mucosa, the associated perigastric adhesions noted at times, and the not infrequent adjacent lymph node enlargement suggest an underlying chronic infection. However, no definite train of events has been established to make this more than a speculative hypothesis.

Symptoms of this condition are not characteristic. Most of our patients have complained of epigastric distress and fullness, but usually the history lacks the characteristic picture so frequently elicited with an ulcerating lesion of the stomach or duodenum, unless associated with this condition. When of short duration, the symptoms suggest those so frequently associated with early gastric malignancy. Anorexia and weight loss have not been an outstanding feature in most cases in our experience, although they have been reported more frequently by others. Severe epigastric pain and tenderness, vomiting, and passing of blood have occasionally occurred. The condition has been found on routine gastric x-ray studies when the patient has been symptom free. The duration of symptoms varies greatly from a few weeks or months to many years.

The diagnosis, or at least the detection, of giant hypertrophy of gastric mucosa is dependent for the most part on the roentgenological findings. Filling defects and irregularity of the lesser and greater curvatures of the stomach, particularly the latter, are the outstanding features. Vaughn and coworkers,[13] using a 36-inch target–film distance, found the average width of the gastric rugae to be 8 mm., determined after two or more examinations not less than a month apart. They also found that peristalsis was sluggish and ineffective and motility of the gastric mucosa limited, with either delayed or absent antral systole.

Gastroscopic examination is of great aid in helping to confirm the diagnosis of giant gastric rugal hypertrophy. However, neither this examination

nor x-ray study may at times rule out the possibility of gastric malignancy. If the services of a competent gastroscopist are available, this type of examination should be resorted to because information may be obtained that has been overlooked by the roentgenologist. Superficial or small areas of ulceration, small polyps, the extent of mucosal involvement, and changes suggesting malignancy may be more apparent to the gastroscopist than to the roentgenologist. Benedict[2] has been successful in obtaining biopsies by the use of the flexible gastroscope that have been of aid in differentiating gastric carcinoma from gastritis. Needless to say, a biopsy showing carcinoma is far more important than one that does not. As Benedict stated, "One should be cautious, however, about putting too much faith in a biopsy showing a nonmalignant process as the value of any endoscopic biopsy depends entirely upon the endoscopist's ability to secure a proper tissue sample. Nevertheless, when a diffuse carcinoma or a lymphoma is suspected, considerable reliance may be placed on a gastroscopic biopsy that does not show it." Since this method of examination seems relatively free of complications, wider application of this diagnostic procedure is no doubt indicated in the hands of those properly trained.

Gastric washings and the abrasive balloon to secure material for cytological study have been used, but since these methods have not been very reliable in attempting to diagnose lesions of the stomach in general, there is little reason to believe, for the time being at least, that they will play a very important role in dealing with suspected gastric mucosal hypertrophy. Browne and co-workers,[4] reporting on 93 cases in which this method of examination was used, stated, "The problem of associated gastritis might be an extremely important factor in the accuracy of cytologic diagnosis since it created the greatest confusion for the pathologist in ascertaining malignant change." They conclude that much remains to be accomplished in the field of cytology as related to the stomach. As clinicians become more familiar with the problem of gastric mucosal hypertrophy, I am sure there will be less difficulty in being fairly confident in the ability to differentiate this condition from some form of gastric malignancy. I am equally confident, however, that certain cases will need to be subjected to exploratory laparotomy before this can be determined with assurance.

The following case reports and the accompanying x-ray reproductions and subsequent discussion illustrate some of the problems encountered in dealing with the subject of giant hypertrophy of gastric mucosa.

CASE REPORTS

CASE 1.—A Japanese man, aged 53 years, was first seen at the Straub Clinic on Dec. 14, 1950, complaining of epigastric fullness and distress of ten months' duration. There had been some loss of appetite and weight but not of much significance. General physical examination was negative. X-ray studies (Fig. 1) showed extensive polypoid gastritis, thought to be benign, but the possibility of malignancy could not be ruled out. Gastroscopy was reported to show a polyp arising in the posterior wall near the mid-portion of the lesser curvature, with large hypertrophic mucosal folds in the region of the mid-portion of the greater curvature. Gastric analysis without histamine showed no free hydrochloric acid and a pH of 7; after histamine, free hydrochloric acid was 4 plus and pH 2.5. Total protein was 5.7 Gm. per cent, globulin 1.7 Gm. per cent, albumin 4 Gm. per cent, albumin:globulin ration 1:2.35.

Since the patient was of a race in which the incidence of gastric malignancy is very high, exploration of the stomach seemed advisable. This was done on Dec. 19, 1950. The stomach showed the typical picture, previously described, of hypertrophic gastritis. No evidence of polyps could be seen after opening the stomach, but giant hypertrophy of gastric mucosa in the mid-portion of the stomach near the greater curvature was evident. Biopsy of the gastric wall in the area of greatest involvement revealed no evidence of gastric malignancy, just the typical picture of mucosal hypertrophy.

None of the stomach was resected. Over the ensuing four and one-half years, the patient has continued to complain intermittently of the same symptoms. Repeated x-rays, the last one on July 28, 1955, show the condition unchanged.

Fig. 1.—Case 1. Showing marked involvement of the proximal two-thirds of the stomach with hypertrophic gastritis. Biopsy negative for carcinoma.

CASE 2.—A Japanese man, aged 37 years, was first seen on Aug. 5, 1952, with symptoms of substernal pressure and epigastric discomfort of two weeks' duration. His symptoms were not related to the intake of food. His father recently had been operated upon for gastric carcinoma. There was slight epigastric tenderness on palpation. Physical examination was otherwise negative.

The x-ray report was as follows: "Extensive diffuse pathology of the stomach with large constant filling defects in the upper third of the stomach near the lesser curvature. There is diffuse hypertrophic gastritis with giant rugae throughout the entire stomach except the antrum. It is believed that this is diffuse hypertrophic gastritis of the giant rugae type with a polypoid tumor of the proximal third. Surgery is indicated since a

carcinoma cannot be ruled out." Gastric analysis before and after histamine showed no free hydrochloric acid and a pH of 5.6. Plasma protein was 6 Gm. per cent, globulin 2.42, albumin 3.60. Albumin:globulin ratio was 1:1.48.

The stomach was explored on Aug. 15, 1952. The stomach wall was thickened on palpation. It had the characteristic feeling of being filled with worms. There was no evidence of a localized lesion. The stomach was freely movable. Through a longitudinal incision in the mid-anterior gastric wall, a thorough investigation of the interior of the stomach was made by inspection and palpation. There was tremendous hypertrophy of the gastric mucosa. The largest ruga causing the filling defect shown in the x-ray study (Fig. 2) was biopsied.

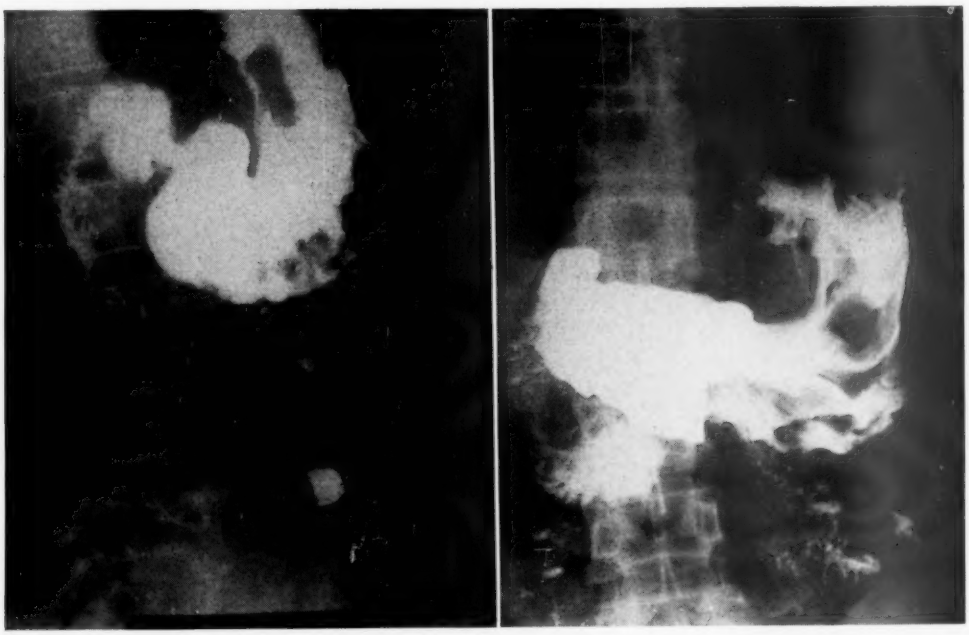

Fig. 2.—Case 2. Filling defects in stomach suggestive of tumor. Biopsy showed only hypertrophic gastritis.

There was no evidence of malignancy, simply the picture of hypertrophic gastritis. To remove the involved mucosa would have required resecting approximately three-fourths of the proximal stomach and this did not seem justified in a young person with minimum symptoms who was engaged in daily hard labor. The patient made an uneventful recovery.

Gastric analysis on Sept. 2, 1952, without histamine, showed free hydrochloric acid 4 plus and a pH of 1.2. Subsequent gastrointestinal studies on Sept. 29, 1952, April 3, 1953, and March 13, 1954, all showed some improvement, and the patient had shown some symptomatic relief.

On Dec. 1, 1954, the patient suddenly collapsed and died as the result of coronary heart disease.

CASE 3.—A Japanese man, aged 41 years, was seen on March 1, 1948, with symptoms of two months' duration of epigastric fullness after eating. He felt miserable all day and was nauseated at times. He did not vomit. His appetite was good. There had been no weight loss.

Physical examination was negative. A gastrointestinal study of March 3, 1948, was reported as follows: "There is an infiltrating lesion involving the body of the stomach along the greater curvature and extending into the posterior wall. Conclusion: Carcinoma of the stomach or extensive gastritis."

Gastric analysis before and after histamine showed no free hydrochloric acid and a pH of 3.5. Gastroscopy on March 9, 1948, revealed extensive gastritis, but nothing that

Fig. 4.—Case 3. Same as Fig. 3, four years later.

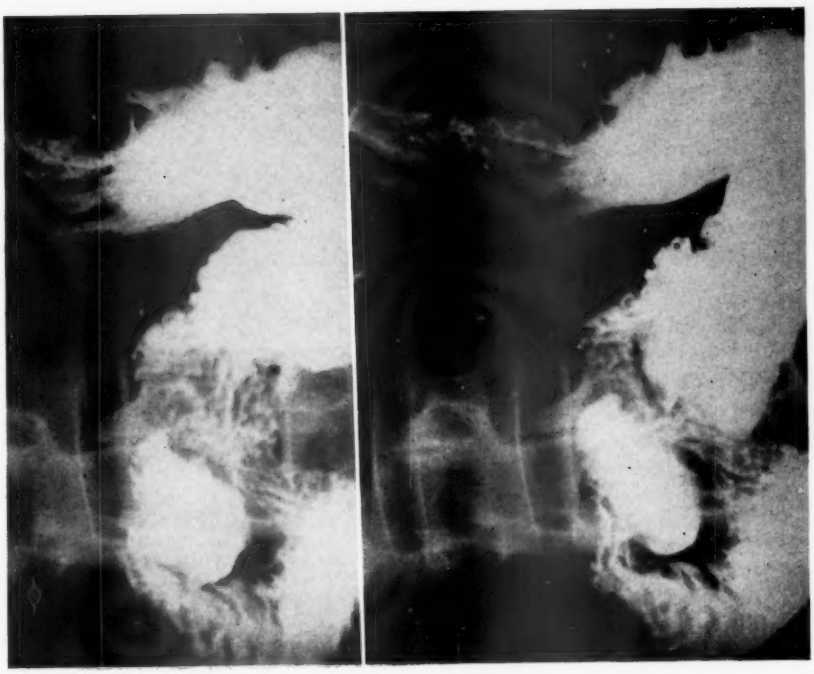

Fig. 3.—Case 3. Hypertrophic gastritis simulating malignancy.

was thought to show malignancy. Re-examination of the stomach was done by x-ray study on March 10 and March 29. There was marked irregularity of the greater curvature and the upper two-thirds of the stomach (Fig. 3).

Since the patient continued to have symptoms with beginning loss of weight and energy, and malignancy could not be ruled out, he was subjected to exploration on April 6, 1948. This revealed nothing suggesting malignancy. Biopsy of the stomach wall showed subacute gastritis. The last x-ray study, July 11, 1952 (Fig. 4), showed the condition to be much the same, and symptoms, when the patient was last seen, on Aug. 15, 1952, were somewhat less marked.

CASE 4.—A Japanese man, aged 40 years, was first seen at the Straub Clinic on Nov. 16, 1954, complaining of stomach trouble. He gave a history of having had an exploration of the stomach five years previously because of symptoms of fifteen months' duration consisting of dull epigastric pain about three hours after meals. The preoperative diagnosis was prepyloric ulcer.

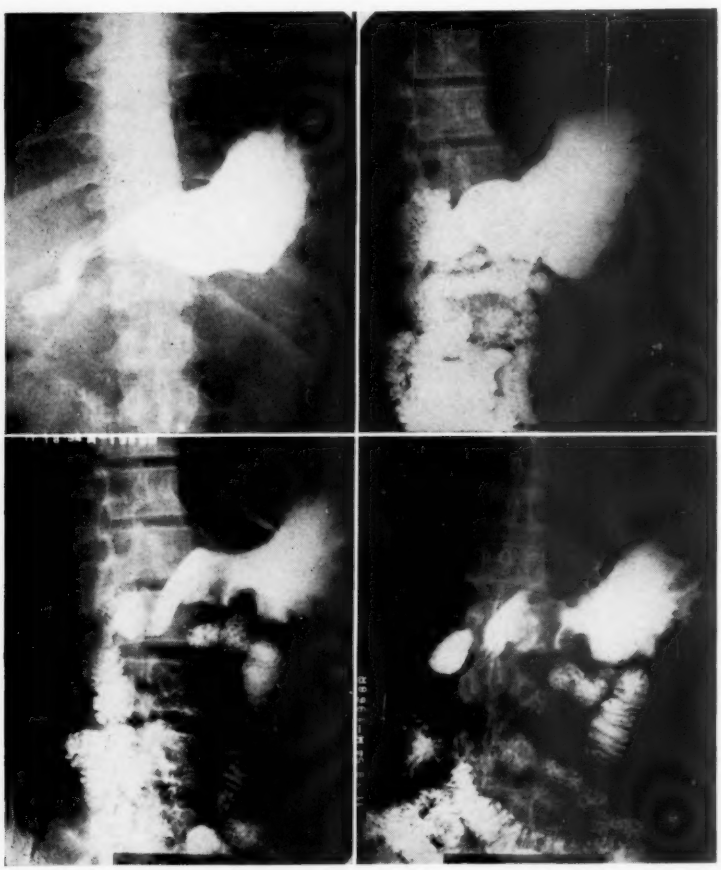

Fig. 5.—Case 4. Upper left; x-ray of stomach, August, 1949. Upper right; April, 1953—diagnosis of hypertrophic gastritis. Below; November, 1954—diagnosis, carcinoma of stomach.

Examination of the stomach at operation, both externally and internally after an adequate incision into its anterior wall, was reported to be negative. The patient remained free of symptoms for one year. He was readmitted to the hospital on Sept. 22, 1953, with a diagnosis of hypertrophic gastritis. Medical treatment resulted in some relief but not for long. The patient was again admitted to the hospital in November, 1954, with a diagnosis of carcinoma of the stomach after x-ray study. Symptoms were difficulty in swallowing of three months' duration with loss of appetite and weight and epigastric discomfort.

At operation, practically the entire stomach was involved with the malignancy. A total gastrectomy was done because of symptoms of obstruction of the terminal esophagus, and, so far as could be told, the lesion grossly had not spread beyond the adjacent lymph nodes. Examination of the gross specimen showed the serosa to be uninvolved. The entire mucosa was intact. No ulceration was present. The gastric wall was involved with adenocarcinoma, giving the typical picture of linitis plastica. The patient died two and one-half months after surgery.

Fig. 6.—Case 5. Hypertrophic gastritis involving practically all of stomach.

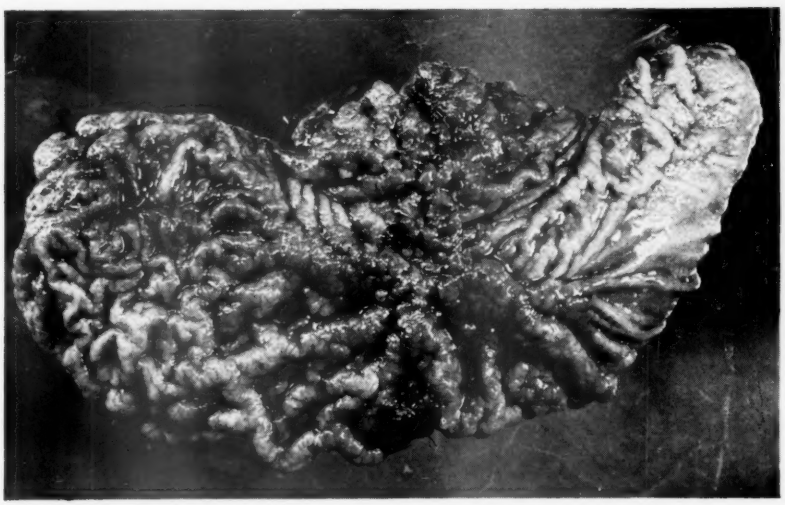

Fig. 7.—Case 5. Photograph of gross specimen after total gastrectomy (x-ray, Fig. 6).

In reviewing this patient's x-rays taken in August, 1949, April, 1953, and November, 1954, one can see the changes that have taken place from a more or less normal-appearing stomach, to one suggesting hypertrophic gastritis, to one, in 1954, showing definite evidence of malignancy (Fig. 5).

CASE 5.—A white man, aged 34 years, was first seen in April, 1948, complaining of epigastric pain of four months' duration, coming on immediately after eating. He was frequently nauseated, though he never vomited. He had lost 15 pounds in weight. He gave a history of having been confined in a German concentration camp during World War II, at which time he was subjected to various studies to determine the effects of vitamins. He had been given very little food and apparently lost a great deal of weight.

Physical examination at this time was essentially negative. Gastrointestinal x-ray (Fig. 6) showed filling defects along the greater curvature of the stomach, interpreted as due to giant hypertrophic gastric rugae. The red blood count was 4,660,000 and hemoglobin 16 Gm. Gastroscopic examination of the pars media at depths II and III and along the greater curvature, and even along the lesser curvature proximal to the angulus, showed huge rugae, some of which appeared to be almost polypoid, being as large as the index finger. The gastroscopist thought that these were probably benign but did not feel carcinoma could be ruled out. Exploration was advised.

This was done on Feb. 16, 1948. The stomach was found to be very large and thick-walled, and very vascular, and had the feeling of being filled with worms on palpation.

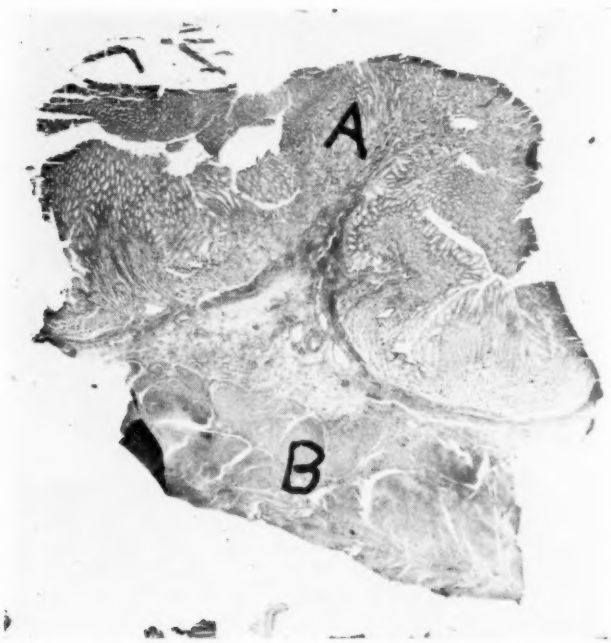

Fig. 8.—Case 5. Giant hypertrophic gastritis. Low-power photomicrograph to show thickening and folding of gastric mucosa (*A*). Musculature (*B*) is moderately thickened. Hematoxylin and eosin (×7).

The wall was pliable everywhere. The serosa was normal in appearance. The gastrohepatic mesentery was greatly thickened. The surrounding lymph nodes were much enlarged. Frozen sections of the lymph nodes and of the gastric wall in the area most involved showed no evidence of malignancy. Examination of the interior of the stomach showed involvement of almost the entire gastric mucosa (Fig. 7). The patient was having so much distress, and had lost so much weight, that it was felt a total gastrectomy was indicated. From this procedure the patient made an uneventful recovery and two months later had gained 21 pounds. Shortly after this the patient left the Territory and his further observation has not been possible.

DISCUSSION

The current literature dealing with giant hypertrophy of gastric mucosa is scant. The almost universal comment in articles discussing this subject is that the condition is rare. Vaughn, Gunter, and Erwin[13] in June, 1951, reported 41 cases showing chronic enlargement and tortuosity of the mucosal folds found on repeated roentgen examinations. Some of these were verified by gastroscopic examination and, when available, the number not stated, by pathologic findings. These were accumulated over a ten-and-one-half-year period from Jan. 1, 1940, and involved 32,640 gastric x-ray examinations on 21,206 patients. Kennedy, Dockerty, and Waugh[6] in July, 1954, stated, "The paucity of established cases reported in the literature attest to the rarity of this condition." Up to that date they had been able to collect only 47 established cases proved either by operative or autopsy findings. To this they added 20 cases coming under observation from 1926 through 1951 in which the diagnosis had been confirmed by biopsy. Berger and co-workers[3] in December, 1954, stated, "Our patient makes the sixty-second substantiated case since Menetrier's original description in 1888." Washko of the Straub Clinic, during a seven-year period ending Sept. 1, 1955, found 118 cases of extensive hypertrophy of the gastric rugae, in which, from his point of view, the possibility of something more serious had to be considered. A number of these cases have been gastroscoped, a considerable number have been re-x-rayed, and five have been subjected to surgical exploration to rule out malignancy. Approximately one-half of the number have occurred in Japanese and those of the giant type have been predominantly in Japanese.

Two laboratory findings, namely, hypoproteinemia and achlorhydria or, at least, diminished hydrochloric acid secretion, have not infrequently been found to be associated with hypertrophic gastritis.

Studies to determine the cause of hypoproteinemia usually found in Menetrier's disease have not been very enlightening. It has been suggested that a substance is produced by the gastric mucosa which exerts an inhibitory influence on the synthesis or storage of protein or that plasma may be lost through the abnormal mucosa into the gastric lumen. Liver function studies and examination of biopsy specimens of the liver fail to suggest this organ as being the primary etiological factor.

Balfour and associates[1] report a patient who failed over a five-month period of intensive medical therapy to show improvement of severe hypoproteinemia but quickly returned to normal following total gastrectomy.

The clinical diagnosis of giant mucosal gastric hypertrophy presents several problems which should be given serious consideration: (1) Is the condition malignant? (2) If not malignant now, is it liable to become so? (3) Should the patient be subjected to exploratory laparotomy, and, if the suspected diagnosis of mucosal hypertrophy is confirmed, what, if any, attempt at surgical correction should be made? (4) What medical measures, if any, in the treatment of this condition are of value, and what follow-up studies should be carried out?

It has been found that a number of gastric lesions may simulate or be confused with giant hypertrophic gastric rugae. Probably the most important

to bear in mind are polypoid and diffusely invading linitis plastica type of cancer, multiple polyposis, lymphosarcoma, and Hodgkin's disease. Most cases, after careful history and physical examination and after x-ray and gastroscopic examination, repeated if necessary, will fall into the category of being in all probability safe to treat conservatively. A few, even in the hands of those most experienced, cannot be diagnosed with assurance, and then, all things being equal, these cases should be subjected to exploration.

Just what surgical procedure should be carried out at the time of exploration, when the lesion has been found to be hypertrophic gastritis, can only be determined at the time, and even then one may be in considerable doubt as to what is the best thing to do. No doubt some cases will be benefited by partial gastrectomy, even total gastrectomy, but in general it would seem rarely necessary to do more than make an adequate biopsy of the gastric wall in order to be sure that malignancy is not present. The characteristic feel of the stomach wall, soft and pliable; the sensation that one is grasping a stomach filled with worms; and the characteristic appearance of the greatly hypertrophied rugae, resembling cerebral convolutions, make it rarely necessary to depend upon the microscopic picture to establish a correct diagnosis, even though this examination should never be omitted. A generous longitudinal incision in the mid-portion of the anterior wall of the stomach is made to permit adequate exploration. The presence of polyps, areas of ulceration, or any abnormality in appearance or to palpation can then be determined and the area either excised or biopsied as seems advisable. A subtotal gastric resection, to completely remove an involved distal segment, is not a procedure to view with alarm. The removal of a proximal segment, or a total gastrectomy, should never be done lightheartedly, because of the serious complicating factors so frequently met with postoperatively. In general, it would seem better merely to establish the diagnosis and leave future problems to be dealt with by conservative measures.

The relationship of gastric mucosal hypertrophy to gastric malignancy is a question that has not been settled. There are certain observations that would seem to indicate that there is a relationship. The incidence of gastric malignancy in Japanese men has been determined to be from two to two and one-half times greater than that in other races living in Hawaii.[12] The incidence of hypertrophic gastritis, we believe, is correspondingly high in this racial group. Case 4 is a proved carcinoma developing along with associated hypertrophic gastritis as revealed by x-ray study. Whether this was coincidental or causative cannot be determined.

As is well known, malignancy of the stomach is commonly associated with achlorhydria. In pernicious anemia this finding is of diagnostic significance, and here carcinoma of the stomach is not infrequently encountered. Polyps of the stomach are recognized as being a premalignant disease and hypochlorhydria is a commonly associated finding. In cases of marked hypertrophy of gastric mucosa, also, it is usual to find a marked deficiency in secretion of hydrochloric acid.

While none of these observations prove anything definitely, taken collectively they strongly suggest that gastric mucosal hypertrophy may predispose

to malignancy. Further observation over long periods of time by repeated x-ray studies and other means of investigation will be required to establish this relationship, if any, more positively.

The medical treatment of uncomplicated gastritis in its various forms and severity is wholly empirical in nature.[10] The usual dietary precautions advised in treating other gastric lesions, the avoidance of alcohol and other mucosal irritants, are no doubt of some value. Replacement therapy to offset the effects of diminished hydrochloric acid secretion and to combat hypoproteinemia when present may result in clinical improvement, though our experience in this respect has not been encouraging. The patient's normal recuperative powers should probably receive most credit when improvement does occur.

CONCLUSIONS

1. Hypertrophic gastritis of the giant rugae type, we believe, occurs more frequently in Japanese than in other races.

2. Its differentiation from other pathologic lesions of the stomach, particularly malignancy, may at times be impossible without exploration, examination, and biopsy.

3. With our present knowledge of this condition, it is probably inadvisable when such patients are subjected to operation to do more than establish the diagnosis unless the patient's symptoms are severe. Partial gastrectomy, even total gastrectomy, may rarely be indicated, however.

4. The role of hypertrophic gastritis as a lesion predisposing to gastric malignancy has not been established. Further observations must be made to determine this point, but from the accumulated data at the present time, it would seem that such a relationship may exist.

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FECAL FAT AND NITROGEN STUDIES IN POSTGASTRECTOMY PATIENTS

The Relationship of Fat and Nitrogen Excretion to Weight Loss and a Comparison Between Billroth I and Billroth II Subtotal Gastrectomies

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ONE of the most significant long-term problems in the postgastrectomy patient in whom the operation has been performed for benign ulcer disease is loss of weight, failure to gain weight, and associated loss of strength. Gastrectomy for peptic ulcer is now being done in ever-increasing numbers and the indication of "chronicity and economic factors" tends to include a much younger age group—thus emphasizing the problem. Rauch[5] in reporting on 700 postgastrectomy patients who were operated upon for benign ulcer indicates that 80 per cent averaged 13.8 pounds below preoperative weight. Other reports in the literature[1, 2, 4] indicate significant weight loss in 30 per cent and over of postgastrectomy patients. At Shaughnessy Hospital recent follow-up studies of partial gastrectomy, and gastrectomy and vagotomy cases re-examined five years after surgery revealed that 27 of 48 patients, or 55 per cent, were an average of 9 pounds below their preoperative weight. The remaining 21 cases had an average weight gain of 11 pounds. Approximately 50 per cent of these follow-up patients stated that there was a significant diminution in their strength postoperatively, so that they had to either change their line of work or found that they could continue their previous work only with excessive fatigue.

The questions then arise: What is the reason for this weight loss and can any particular type of gastrectomy or changes in postoperative management do anything to prevent or correct weight loss? The problem resolves itself, we believe, into two factors: first, is weight loss simply due to the fact that the postgastrectomy patients cannot eat enough food or take food of sufficient caloric value to enable them to maintain normal body weight and supply them with energy for any desired type of work? Second, is the weight loss and loss of strength, in part at least, due to a disturbance in the digestive process? If the chief factor is that the size and function of the remaining gastric pouch will not allow the patient to take sufficient food to supply energy for any desired type of work, then the problem can probably never be solved, for it has been proved by experience that we cannot compromise with the amount of stomach resected

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if we are to cure the patient of his ulcer disease and prevent recurrence. We do feel that the surgeon should strive for a balance in an attempt to judge that fine point where enough stomach is resected to ensure cure and yet a pouch remains of a size sufficient to enable the patient to maintain eating habits as nearly normal as possible. If the weight loss and loss of strength, in part at least, is due to a disturbance in the normal digestive process, then the logical question arises as to whether any particular type of gastrectomy and anastomosis is more liable to maintain a more normal digestive process postoperatively. In recent years there has been, in many centers, a return to the Billroth I type anastomosis. Reports[3] from some of these centers state that weight is better maintained postoperatively in these patients.

With all of these factors in mind, we set out at the Clinical Investigation Unit at Shaughnessy Hospital to attempt to answer the following three questions: (1) Are there significant measurable abnormalities in digestion in postgastrectomy patients, (2) if such abnormalities are present, can weight loss be directly related to them, and (3) if such abnormalities are present, do they vary in Billroth I and Billroth II type gastrectomies?

To attempt to measure abnormalities in the digestive process in patients who are not in a grossly abnormal state is difficult. However, it is felt that one of the more reliable yet relatively simple methods of estimating the efficiency of an individual's digestive process is by analysis of stool for fat and nitrogen with the patient on a carefully controlled diet. Wollaeger and Comfort, and their associates[6] in 1946, reported such studies on normal and postgastrectomy patients. Their figures for fecal fat excretion are as follows: (1) normal fecal fat is usually below 5 per cent of the ingested fat; (2) excretion of over 10 per cent of ingested fat is definitely abnormal; and (3) excretion of between 5 per cent and 10 per cent of ingested fat can be classed as borderline.

Nitrogen excretion on any diet should never exceed 2 Gm. per day. Wollaeger's values for fat and nitrogen excretion have been accepted by many other workers[4] as a basis for further study. Wollaeger was also able to show that benign disease of the stomach and duodenum did not affect fat and nitrogen excretion. We studied 3 patients with peptic ulcer disease who had not been operated upon as controls. These patients showed an average fat excretion of 4 per cent of ingested fat and an average nitrogen excretion of 1.3 Gm. per day. We therefore concluded that Wollaeger's values would be applicable in our study.

METHOD

In our present study 20 patients who had had a partial gastrectomy for benign peptic ulcer were used; 10 of these patients had had a Billroth II anastomosis (chiefly postcolic Hoffmeister modification of the Polya) and 10 patients had had a Billroth I anastomosis. In addition, a total of 5 of these patients had had vagotomy combined with partial gastrectomy. All patients were at least one year postoperative and the average patient was three years' postoperative. All patients could be classed as at least a fair to good postgastrectomy result. In neither group was there included any patient with dumping syndrome of any severity or other postgastrectomy complaint. It was felt that our total group represented a fair cross section of postgastrectomy patients and that neither individual group contained patients in whom results of study might weigh favorably or unfavorably toward their respective group.

Patients were admitted to the Clinical Investigation Unit of Shaughnessy Hospital. A careful history of their preoperative state and postoperative course, with particular regard to pre- and postoperative digestive symptoms, weight, strength, work, and social history was taken. Complete physical examinations were done. The patients were placed on a diet that averaged approximately 2,700 calories per day and each patient's tolerance of food was pushed as far as possible, short of giving any postprandial distress, nausea, and so forth. In this way we hoped to be able to determine in a sense the food capacity of these patients. Each patient was given as close to 150 Gm. of fat per day as he could tolerate. All food ingested and any returned on the trays was carefully evaluated by a dietitian. Patients, after four days of this controlled diet, were given a marker capsule containing carmine red. On the fourth day following this first capsule and while continuing on the same diet the patients were given a second marker capsule. Stools excreted following the first marker capsule and until the second marker capsule appeared were collected and the fat and nitrogen contents measured.

RESULTS

Clinical Evaluation.—This group is too small to make any definite conclusions regarding any difference between Billroth I and Billroth II type gastrectomy patients. There appeared, however, to be very little difference in any digestive symptoms in the two groups; the incidence of mild dumping syndrome was about the same and in the groups studied there were no patients with evidence of severe dumping. There did not appear to be any over-all difference in strength in the two groups of patients, although two of the Billroth I patients were carrying on extremely heavy manual labor, while none of the Billroth II type patients were able to do such labor, although some had done such preoperatively.

Table I lists the Billroth I group of 10 patients in order from the one losing the greatest percentage of weight as compared to the preoperative state to the one gaining the greatest percentage of weight. Fecal fat excretion, fecal nitrogen excretion, and the average daily caloric intake are listed.

TABLE I. BILLROTH I

	VAGOTOMY	WEIGHT (%)	FECAL FAT (%)	GRAMS FECAL NITROGEN	AVERAGE DAILY CALORIC INTAKE
1	✓	- 9.1	8.4	2.0	2666
2		- 8.1	6.7	1.5	2632
3		- 6.5	5.8	1.7	2538
4		+ 0.6	3.3	1.0	2686
5		+ 3.4	2.9	2.0	2780
6		+ 5.3	2.5	1.9	2752
7		+ 7.4	3.4	1.2	2837
8	✓	+ 7.6	21.7	3.6	3387
9		+ 9.5	3.9	1.8	2754
10	✓	+19.4	5.8	2.4	2704
Average			6.4	1.9	

Table II similarly gives the results in the Billroth II patients. The patients who had vagotomy in addition to gastrectomy are indicated.

On comparison of the two tables, it is first noted that there is no significant difference in the number of patients in each group who had lost weight or in the range of weight loss or gain. It is also apparent that there is no significant difference in the range of fecal fat and nitrogen values, except for one patient;

TABLE II. BILLROTH II

	VAGOTOMY	WEIGHT (%)	FECAL FAT (%)	GRAMS FECAL NITROGEN	AVERAGE DAILY CALORIC INTAKE
1		-12.3	8.3	1.9	2657
2		-10.1	3.9	2.8	2826
3		- 9.3	5.8	2.5	3175
4		- 3.9	3.6	1.7	2066
5	✓	0	5.8	2.0	2700
6		+ 1.9	6.0	2.0	3037
7	✓	+ 3.3	10.8	2.3	2554
8		+ 5.3	2.8	2.0	2711
9		+ 5.6	5.7	1.2	2576
10		+ 6.5	11.7		2716
Average			6.4	1.9	

Case 8 listed in Table I. This patient was somewhat unusual in that fecal fat of 21.7 per cent would indicate a state of steatorrhea and one might expect symptoms of such. Such was not the case however in that this patient's bowel movements were normal in amount and frequency. His weight had increased 7.6 per cent postoperatively and at the time of study he was six feet tall, weighed 189 pounds and was doing extremely heavy work as a millwright. The majority of the individual cases seem to show some balance between fat excretion, nitrogen excretion, and caloric intake, which might account for weight gain or loss. It is perhaps significant that the group of Billroth I patients who gained weight, with the exception of Case 8, all had normal or very low borderline fecal fat values and caloric intake above average, while those who had lost weight all had borderline fecal fat values and a lower caloric intake. Such is not the case in the Billroth II group and this might suggest that in the Billroth II patients, with a short-circuited upper gastrointestinal tract, there is a varying ability to readjust following gastrectomy and fat and nitrogen excretion may vary with this adjustment. Let us now consider some of the individual factors.

Weight loss: Of the entire group of 20 patients, 7 had lost weight compared to their preoperative levels. Four of these were from the Billroth II group and they lost an average of 8.8 per cent of their preoperative weight. Three patients were of the Billroth I group and the average loss was 7.9 per cent. There is therefore no significant differences in the number of patients losing weight in the two groups, nor in the average weight loss. Examination of the tables also reveals that there is no significant difference in the amount of weight gain in the two groups.

Caloric intake: The average daily caloric intake of the entire group was 2,737 calories per day with a range of from 2,066 to 3,387. It is apparent that there was a significant variation in the eating capacity of the patients studied. From the tables it is seen that there is no significant difference in the average caloric intake between the two groups. It is apparent that those patients in both groups who gained weight, in most instances, had a caloric intake exceeding that of those patients who had lost weight.

Fecal fat: The average fecal fat excretion of the entire group was 6.4 per cent of ingested fat, which would place the average postgastrectomy patient in

this study in the borderline group. The Billroth I group averaged 6.4 per cent of fat excretion and the Billroth II group also averaged 6.4 per cent. It is an unusual coincidence that the average fat excretion in the two groups is identical. Table III indicates the number of patients in each group according to the classification of normal, borderline, and abnormal fat excretion. Again we see that there is no significant difference in the two groups. It is interesting to note that none of the three patients with abnormal fat excretion (10.8 per cent, 11.7 per cent, 21.7 per cent) were below their preoperative weight. Of the 7 patients who had lost weight, 2 had normal fat excretion and five borderline levels. There does not therefore appear to be any relationship between fat excretion and weight loss or weight gain.

TABLE III. FECAL FAT EXCRETION (20 CASES)

	NORMAL	BORDERLINE	ABNORMAL
	0-5 PER CENT	5-10 PER CENT	10 PER CENT
Billroth I	5	4	1
Billroth II	3	5	2
Total Series	8	9	3

Nitrogen excretion: The average nitrogen excretion of the entire group was 1.9 Gm. per day and each of the Billroth I and Billroth II groups averaged 1.9 Gm., again an unusual coincidence. In Table IV the nitrogen excretion of the two groups is indicated and shows those patients with a nitrogen excretion of below 2 Gm. per day which is normal, those patients with a level of 2.0 Gm. which is upper limit of normal and those above 2 Gm. Again there is no significant difference in the nitrogen excretion of the two groups of patients. It is apparent that in the total series there is a definite tendency to increased nitrogen excretion, although only a minority shows levels that are definitely abnormal. Only 2 of the patients with abnormal nitrogen levels had lost weight. Therefore, there does not appear to be any distinct relationship between nitrogen excretion and weight gain or loss.

TABLE IV. FECAL NITROGEN (19 CASES)

	BELOW 2.0 GM.	2.0 GM.	ABOVE 2.0 GM.
Billroth I	6	2	2
Billroth II (9 only)	3	3	3
Total Series	9	5	5

Effects of vagotomy: In the entire group, there were 5 patients on whom vagotomy had been performed in addition to partial gastrectomy, 3 associated with a Billroth I procedure and 2 with a Billroth II. Table V indicates the relationship of fat and nitrogen excretion to vagotomy. It is to be noted that 2 patients showed abnormal fat and nitrogen excretion and one additional patient had abnormal nitrogen excretion alone. None of these patients had normal fat excretion. However only one patient who had had vagotomy and gastrectomy showed weight loss. We must conclude that vagotomy in addition to partial gastrectomy definitely increases fat and nitrogen excretion.

TABLE V. VAGOTOMY (5 CASES)

	FAT		NITROGEN	
	BORDERLINE	ABNORMAL	2.0 GM.	ABNORMAL
Billroth I (3 cases)	2	1	1	2
Billroth II (2 cases)	1	1	1	1
Total 5	3	2	2	3

DISCUSSION AND CONCLUSIONS

Metabolic studies in the form of fecal fat and nitrogen excretion studies were done on 20 postgastrectomy patients who had been operated upon an average of three years previously for benign peptic ulcer disease and who had good postoperative results. Ten of these patients had had a Billroth I subtotal gastrectomy and 10 a Billroth II type subtotal gastrectomy. A total of 5 patients had had vagotomy combined wih subtotal gastrectomy. Seven of these patients were below their preoperative weight (28 per cent), but there was no significant difference in the number losing weight in the two groups. Neither was there significant difference in the number gaining weight or the amount of weight gained in the two groups. From our studies of fat and nitrogen excretion on controlled diet we would agree with the consensus of other workers. There is a definite tendency to an elevation of fat excretion and of nitrogen excretion in postgastrectomy patients. However, in the majority of cases the elevation is only to a borderline level and only a few cases show elevation to abnormal levels. There does not appear to be any direct relationship between elevation of fat and nitrogen excretion and weight loss. Our studies suggest that in postgastrectomy patients the food intake is probably the most significant factor in weight gain or weight loss. Vagotomy accompanying partial gastrectomy appears to be definitely associated with increased fat and nitrogen excretion. On comparing Billroth I and Billroth II type postgastrectomy patients, there is no significant difference as a group as regards to increased fat or nitrogen excretion. It is our purpose now to study a group of patients both before and after gastrectomy to determine if there are any significant changes in the individual which may account for weight loss following gastrectomy.

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ACUTE HEMORRHAGIC GASTRORRHEA: ONE TYPE OF ACUTE DILATATION OF THE STOMACH

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ACUTE dilatation of the stomach is a serious complication which develops after a wide variety of operations and other traumas; it is therefore of interest not only to the abdominal surgeon. However, study of the relevant literature shows that acute gastric dilatation is an ill-defined entity. It in fact results from a variety of disorders, three of which are of outstanding importance, namely, mechanical intestinal obstruction, adynamic ileus, and hemorrhagic gastrorrhea.

In all of these, the volume of vomitus or short-tube aspirate is excessive and, unless fluid and electrolyte losses are energetically replaced parenterally, severe and even fatal constitutional symptoms rapidly supervene. In present-day clinical practice, thanks to the basic contributions of Haden and Orr[1] (1924), Gamble and Ross[2] (1925), and Dragstedt and Ellis[3] (1930) such severe systemic effects should be, and generally are, anticipated and prevented; they will not be dealt with in detail here.

We suggest that as a sole diagnosis, "acute dilatation of the stomach," is generally inadequate; the clinician's thinking should reach out to the cause and variety of the gastric dilatation confronting him. The differentiation of mechanical obstructions with backing up of contents and dilatation of the proximal bowel is of the first importance. This paper attempts to go further and to differentiate acute hemorrhagic gastrorrhea, an active, hypersecretive process, from gastroduodenal and more extensive degrees of ileus, in which, we suggest, passive pooling of secretions and ingesta is responsible for the large volumes of aspirate. This distinction is made from the physical and chemical properties of the aspirate.

In the past, curiously little effort has been made to define the character of the aspirate in conditions associated with acute gastric dilatation. Indeed not much has been added to our knowledge of the local pathology since Morris'[4] lucid description in 1883 of a fatal case and his concluding remark, "it is to be regretted that no analysis was made of the vomited matter in this case," gives point to these studies.

METHODS

In a series of patients undergoing a variety of surgical operations, a Levin tube was passed into the stomach and connected to a Wangensteen continuous-suction apparatus.

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Serial 12-hour samples of aspirate were analyzed. Electrolyte and other determinations were done on each 24-hour urine, and estimations of the serum electrolytes, blood urea, and plasma-CO_2 combining power were carried out, though less frequently, to control the adequacy of the intravenous therapy.

The patients were re-examined frequently and progress notes were made, so that the clinical features and the characters of the aspirate could be correlated. The volume and other physical characteristics of each 12-hour specimen were noted but, because of the heavy amount of biochemical work involved, electrolyte and other estimations were sometimes done on only one 12-hour sample from each day, or the two samples were pooled and the chemistry of the 24-hour specimen was determined.

Control data in light of which the findings in acute gastrorrhea may be studied were obtained from two sources.

1. *Pre- and Postoperative Aspirate Volumes.*—The patients in this group, 40 in number, underwent elective operations including appendectomy, colostomy, cholecystectomy, and incisional herniorrhaphy; all recovered without obstructive or other complications. Up to three 12-hour samples of aspirate were obtained on successive nights before operation. During the day the patients were given a nutritious semifluid diet but nothing was allowed after 5 P.M. Shortly before 9 P.M. a Levin tube was passed into the stomach which was then emptied. The tube was connected to a Wangensteen apparatus and the gastric contents were aspirated continuously from 9 P.M. to 9. A.M. At 9 A.M., the suction was disconnected but the tube was left in situ, the patients being allowed to eat until 5 P.M., and to take exercise. At 9 P.M., after emptying the stomach, aspiration was recommenced, a further 12-hour nocturnal sample being obtained.

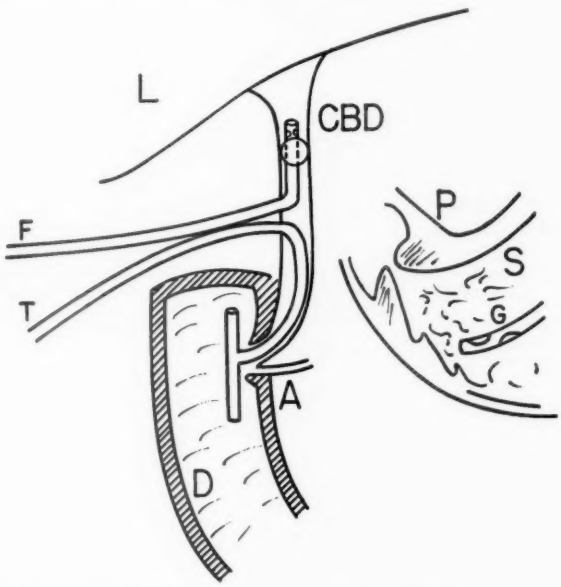

Fig. 1.—Separate collection of bile, duodenal, and gastric aspirates after transduodenal choledochostomy. Cuffed catheter in bile duct, T-tube in duodenum, Levin tube in stomach. *A*, ampulla of Vater; *D*, duodenum; *CBD*, common bile duct; *L*, liver; *P*, pylorus; *S*, stomach; F, Foley catheter; T, T-tube; G, Levin tube (see text).

At operation it was generally possible to establish that the tube lay correctly in the stomach and in other cases this was verified by x-rays, a band of radiopaque material being incorporated in the tip of the tube to facilitate its location. Where the tip had passed on into the duodenum the data were excluded from this paper.

Continuous aspiration was commenced on the patient's return from the operating room, the first 12-hour period being timed from 6 P.M. on that day. It was maintained for

as many days as practicable without causing undue discomfort. Nothing was allowed by mouth but all fluid and electrolyte losses were budgeted carefully and promptly replaced intravenously so that the patients remained in good balance.

From this group of patients only measurements of aspirate volume are given (see Fig. 2). It may be noted, however, that the biochemical studies of their aspirates support the conclusions reached from other data in this paper.

2. Separate Collection of Bile, Gastric, and Duodenal Aspirate.—In a second group of patients with common duct stones this was effected by a modification of McBurney's transduodenal ampullary choledochostomy (Fig. 1).

After checking the position of the intragastric tube, the vertical limb of a fine T-tube was pulled up and out through the choledochostomy opening, the transverse limb lying snugly in the duodenum. A small Foley type of catheter was then passed up the common duct, its distal end being brought out alongside the T-tube. Inflation of the cuff of the Foley catheter ensured that all the bile secreted was drained externally and measured. Thus gastric contents, bile, and duodenal (mainly pancreatic) secretions could be collected separately, via the Levin and T-tubes, and the Foley catheter.

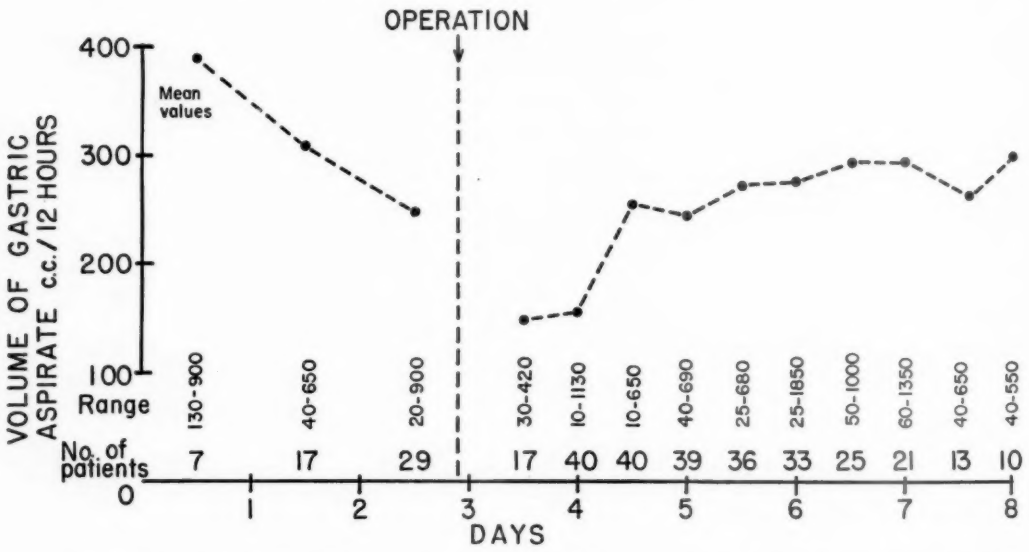

Fig. 2.—Volume of gastric aspirate drained in 12-hour periods before and after sundry operations, from which the patients made uneventful recoveries. Mean 24-hour volumes may be derived by adding two consecutive points.

Chemical methods: Sodium and potassium contents were determined with the Perkin-Elmer flame photometer (Model 52C) and the chloride content by the method of Schales and Schales[5] (1941). The pH was determined with standard litmus papers. Bilirubin concentrations were determined by the method of Powell[6] (1944). For estimation of the blood urea, whole blood was incubated with urease and the resultant ammonia estimated by direct nesslerization of the protein-free filtrate. The CO_2-combining powers were estimated by incubating acidified plasma in Conway vessels with a solution of standard alkali in the center chamber, the alkali being titrated back with standard acid at the end of forty-five minutes. Tests for occult blood were by the routine benzidine method.

RESULTS

Average Volume of Postoperative Gastric Aspirate.—Fig. 2 gives the average volume of aspirate and the range in the values for 12-hour periods before and

after operation. There appears to be a fall in the average volume approaching the operation but the duration and number of the preoperative observations are too small to permit of any firm conclusion in this sense.

On the other hand, it is clear that factors associated with the operation do greatly depress the volume of aspirate recovered afterward. Such factors may include psychic reactions, anesthetic and other drugs (Johnson and Mann,[7] 1942), operative manipulations, and the exposure and cooling of organs. Five days after operation the average volume of the aspirate had risen to a level of 550 to 600 c.c. per 24 hours.* But in the immediate postoperative period it was reduced to about one half of this amount.

As is well known, a mild degree of ileus usually follows abdominal operations and this in itself should favor an increased recovery of aspirate because of passive pooling of the gastroduodenal contents. However, the average aspirate volume after operation is low, which suggests that there is usually some inhibition of gastroduodenal secretory function.

Properties of Separated Bile, Duodenal, and Gastric Aspirate.—These are shown in Table I. It is clear that the reaction and electrolyte pattern of bile and duodenal aspirate are similar. But bile (or a mixture of bile and duodenal aspirate) can be distinguished from pure duodenal aspirate by the absence of bilirubin from the latter.

TABLE I. PROPERTIES OF SEPARATE GASTRIC ASPIRATE, DUODENAL ASPIRATE, AND BILE OBTAINED BY DIFFERENTIAL DRAINAGE AFTER CHOLEDOCHOSTOMY

	GASTRIC ASPIRATE		DUODENAL ASPIRATE		BILE	
ODOR	Nil		Foul and very offensive		Fishlike, slightly offensive	
COLOR (SUPERNATANT)	Colorless		Colorless		Deep yellow	
DEPOSIT	White floccules		White floccules		Nil or occasional fine floccules	
	RANGE	MEAN (NO. OF OBS.)	RANGE	MEAN (NO. OF OBS.)	RANGE	MEAN (NO. OF OBS.)
Vol. c.c./24 hr.	100-1100	540 (31)*	30-520	224 (25)	110-1100	372 (35)
pH	< 2.5	< 2.5 (17)	6.4-8.3	7.9 (19)	6.7-8.2	7.5 (17)
Free acid c.c. N/10 HCl	28-65	42 (17)	nil	nil	nil	nil
Sodium meq./L.	31-88	55 (21)	88-138	123 (19)	120-150	134 (25)
Potassium meq./L.	8.3-17	12.1 (19)	3.8-6.9	5.8 (17)	4.3-6.4	4 8 (25)
Chloride meq./L.	96-142	128 (18)	78-118	100 (20)	107-131	118 (27)
Bilirubin concentration mg. per cent	—	nil	—	< 0.5	25-350	122 (120)†

*Observations were made during first five days after operation in 7 patients. The figure in brackets is the number of 24-hour samples from which mean was derived.

†The data were obtained during the first five days during which bile secretion is much reduced in amount (Rundle et al.[11] 1955). Later, with restoration of normal bile flow, the mean bilirubin concentration in the bile falls to some 30 mg. per cent.

It is also seen that the bilirubin concentration in bile is very high in the immediate postoperative period; relatively small additions of such bile (even diluted with duodenal fluid) would suffice to provide easily measurable concentrations of bilirubin in the gastric aspirate. Clearly the presence of bilirubin in the short-tube aspirate signifies the mixing of duodenal with stomach contents by pyloric reflux.

*This is distinctly lower than the rate of secretion found by Levin and his co-workers[8] (1948) in normal healthy subjects but is of the same order as found after operations by Hardy[9] (1951) and by Eade, and his associates[10] (1955).

Pure gastric aspirate* and duodenal contents† differ markedly in respect of their odor, reaction, and sodium and potassium concentrations. The former is characterized by its very faint odor and high free acidity, and its high potassium but low sodium concentrations. In duodenal contents, a generally inverse pattern is found.

Hence, it is possible to distinguish a "gastric" or a "mixed" pattern in material aspirated from the stomach.‡ Thus, from the physical and chemical characters of a particular specimen we can usually infer its chief site of origin. For example, even in the presence of bilirubin, high free acid, chloride and potassium concentrations associated with low sodium and pH levels would indicate a predominantly gastric origin for the specimen.

Comparison of Table I and Fig. 2 shows that the mean volume of pure gastric aspirate is almost as great as the mean 24-hour volumes recovered in sundry controls. This suggests that in the postoperative fasting patient only minor amounts of duodenal fluid regurgitate into the stomach. In other words, the biliary and duodenal secretions which together are equal in volume to the pure gastric aspirate (Table I) must largely find their way on into the absorptive gut even in the days immediately after abdominal operations, in patients recovering normally.

Changed Pattern of the Aspirate After Gastrojejunostomy.—The foregoing observations are confirmed and illustrated by what happens to the pattern of the aspirate after gastric resection as in the following typical case (Case 1):

A man, aged 49, suffered from a large simple ulcer of the lesser curvature causing gross deformity of the stomach, as established by opaque meal examination. Gastric emptying was hindered, marked retention of barium being demonstrable forty-eight hours after the meal. A subtotal gastrectomy was done with Hofmeister valve gastrojejunostomy. At operation, the Levin tube was carefully adjusted to lie only in the stomach remnant and fixed securely in position.

The physical and chemical characters of serial 12-hour specimens of aspirate are shown in Fig. 3. It is seen that before operation the aspirate had a typically gastric pattern, namely, a low pH, low bilirubin and sodium concentrations, and high chloride and potassium concentrations. The virtual absence of bilirubin was in keeping with the high degree of pyloric obstruction present. The only special feature was the sour odor of the aspirate which could be explained by gastric retention.

After operation, the aspirate was foul-smelling and its biochemical pattern was completely changed, being mixed, but predominantly duodenal in character. Thus, there were a high pH, high bilirubin and sodium concentrations, and a low potassium concentration. It may be inferred that the anastomotic stoma was widely patent.

*This expression is used in the sense, gastric juice uncontaminated by duodenal juices or bile; but the presence of swallowed saliva or sputum is not excluded.

†"Duodenal contents" signifies a mixture of bile, pancreatic, and duodenal secretions, unmixed with gastric juices.

‡Where the physical and chemical characters are those of a mixture of gastric juice and duodenal contents the aspirate is described as "mixed."

A noteworthy, if incidental, feature is the low concentration of bilirubin in the gastric aspirate for forty-eight hours after operation. We have observed this repeatedly after subtotal gastrectomy and the phenomenon may

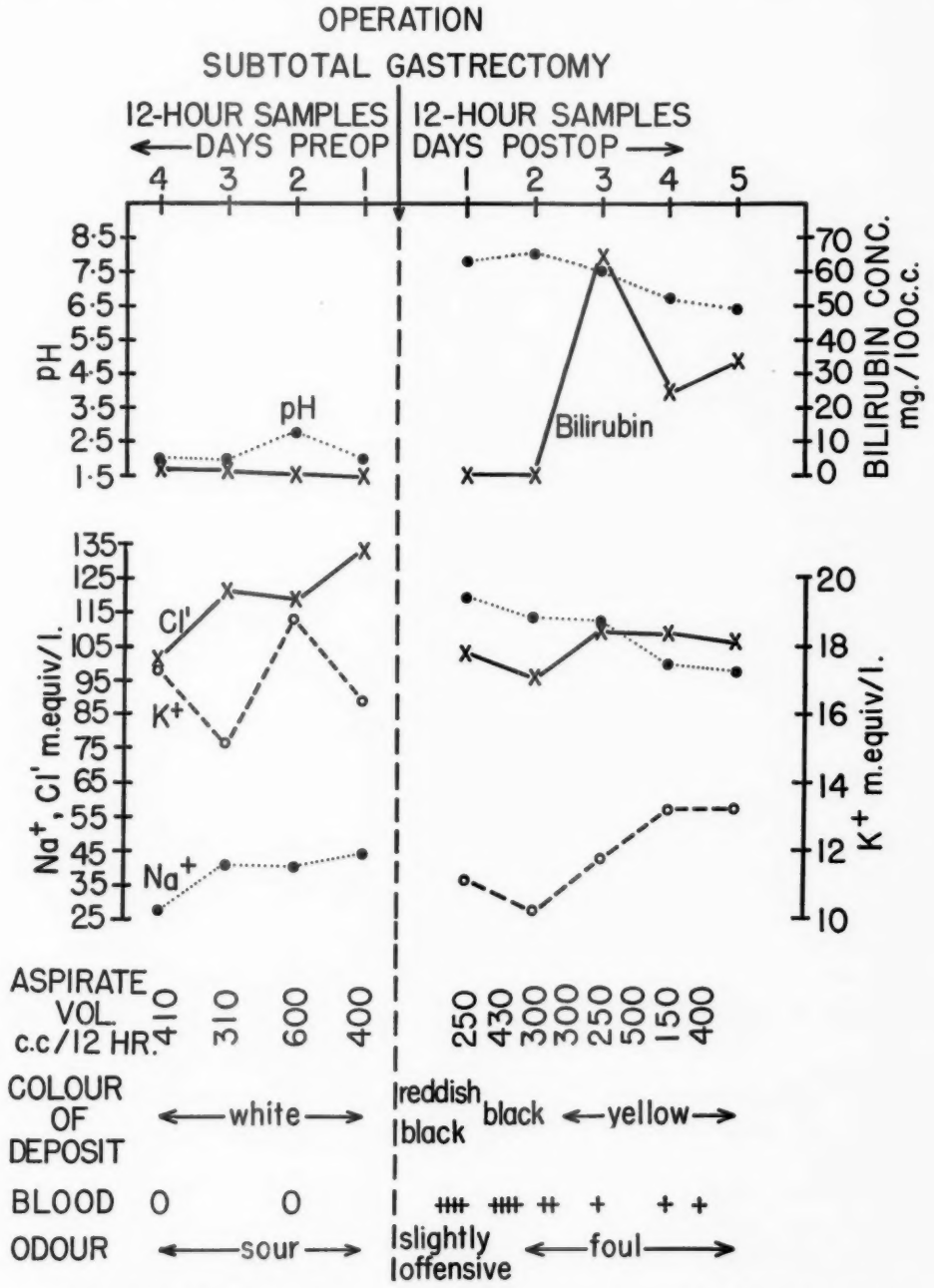

Fig. 3.—Pyloric obstruction treated by subtotal gastrectomy. Data from Case 1. Change in biochemical pattern of short-tube aspirate from gastric (before operation) to mixed, chiefly duodenal (after operation).

derive from an associated depression of biliary secretion. It is known that after operations on the bile passages, there is generally a marked reduction in bile flow (Rundle and his associates,[11] 1955).

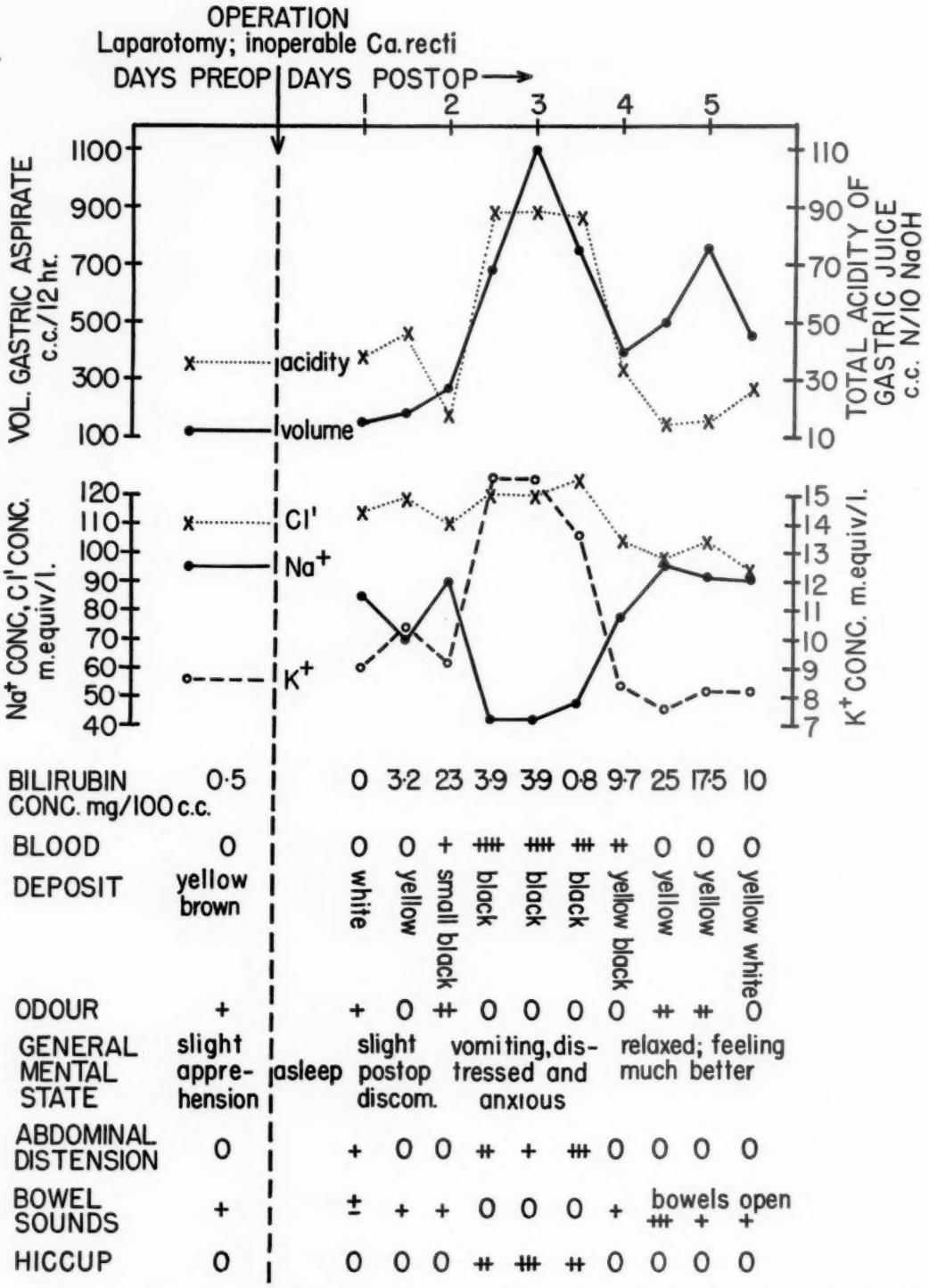

Fig. 4.—Chemistry of 12-hour samples of gastric aspirate before and after operation in a patient who developed acute gastrorrhea and the associated clinical data (Case 2). On third postoperative day, chemical estimations were done on a pooled 19-hour sample.

The Aspirate in Acute Hemorrhagic Gastrorrhea.—A unique opportunity to observe the secretory upset was afforded in a male patient, aged 69, who unexpectedly developed acute hemorrhagic gastrorrhea while control observations were being made on his pre- and postoperative aspirate. Thus full data were obtained on the aspirate before, during, and after its occurrence (Case 2, Fig. 4).

A simple exploratory laparotomy had been done for carcinoma of the rectum, and the growth being deemed inoperable, the wound was closed without establishing a colostomy.

He had tolerated the Levin tube well but was beginning to find it uncomfortable thirty-six hours after operation. It was therefore clamped, with a view to removing it soon afterward.

The aspirate sample immediately preceding this contained much bile and a small amount of black deposit, which was noted as unusual but its significance was not at once appreciated. While the Levin tube was clamped, drinks, including an egg flip, were given and these he promptly vomited. Aspiration had been discontinued at 6 A.M. and by 11 A.M. his upper abdomen was distinctly distended and hyperresonant. Bowel sounds could not be heard. He appeared flushed and restless, and complained of abdominal discomfort and hiccup.

The tube was therefore unclamped and reconnected to the suction apparatus. In the process, gas was heard gurgling out through its lumen and the patient volunteered the information that his abdomen at once felt more comfortable. Thereafter for thirty-six hours the aspirate was profuse and jet black. It flowed at the rate of 2 L. per 24 hours as compared with a maximum of 450 c.c. per 24 hours previously.

Its appearance was distinctive. Its color was due to evenly distributed jet black floccules. When a sample was centrifuged, the floccules compacted to a small black deposit, the supernatant being tinged dark, odorless, and free from turbidity. The deposit dissolved in concentrated sulfuric acid, giving a pink solution which showed bands of acid porphyrin on spectroscopic examination. This in turn was taken up into neutral ether when bands of protoporphyrin were seen, confirming that the deposit was altered blood.

While this abnormal aspirate continued, bowel sounds remained absent, the abdomen was moderately distended, and he was distressed by persistent hiccup. Twenty-four hours after recommencing aspiration the tube was again clamped for a 2-hour test period. His discomfort and distention promptly recurred. When unclamped the tube again transmitted gas audibly and he experienced relief. The aspirate continued black for a further twelve hours but then rapidly took on a normal clear appearance, with white or yellow floccules and some supernatant frothy sputum. Bowel sounds became numerous; he defecated spontaneously. Hiccup and distention subsided.

Fig. 4 summarizes the chief clinical and biochemical findings before, during, and after he developed this complication. Beforehand, the aspirate

samples were a mixture of gastric and duodenal contents, the electrolyte concentrations lying about midway between the mean levels in pure gastric aspirate and duodenal contents (see Table I); and the bilirubin concentration in the preceding 12-hour specimen was 23 mg. per cent.

During the period characterized by profuse bloody aspirate, general malaise, epigastric discomfort, and hiccup, the bilirubin content fell to 0.8 mg. per cent, the curve of acidity rose sharply parallel with the volume increase, and the electrolyte pattern became typically gastric. Afterward, as the aspirate cleared, its volume fell, its biochemical pattern reverted to a mixed one, and the clinical signs abated.

Comment. The patient's stomach was never allowed to become grossly dilated and the prompt recommencement of continuous suction prevented the vomitus from becoming voluminous. The duration of the gastrorrhea was minimal.

In another patient (Case 3, Fig. 5), the circumstances were more usual in that hemorrhagic gastrorrhea was already well established when he was first seen in consultation. The aspirate data, though not so complete, agreed fully with those from Case 2. The patient, aged 65, had undergone a retropubic prostatectomy four days previously. The peritoneal cavity was not entered.

Fig. 5 summarizes the chief clinical and biochemical data. Hiccuping was noticed on the day following operation and became progressively more severe. On the third postoperative day black fluid began to regurgitate through his mouth and nose when he hiccuped and during the evening, while hiccuping, he vomited about 120 c.c. of blood-stained fluid. The nurse then passed a Levin tube*; 420 c.c. of black fluid was aspirated at once and a further 1,100 c.c drained by 6 A.M. on the following morning.

At the height of the process (on the eighth postoperative day) over 2 L. of aspirate were recovered in twenty-four hours. Throughout it was black or very dark red. So much blood and mucus were present that a deposit (altered blood) rarely separated in the aspirate bottle, the contents generally remaining opaque throughout. But when poured on a white tile, the characteristic flocculi of ropy mucus coated with black altered blood were seen. Analysis of the supernatant, after centrifuging a typical sample, showed it to have a purely gastric pattern. Its acidity was high (free acid equal to 42 c.c. N/10 HCl per 100 c.c.), as were the potassium (16.4 meq./L.) and chloride (135 meq./L.) concentrations. The bilirubin content was less than 0.1 mg. per 100 c.c. It was odorless.

Parenteral therapy had not been adequate and there were an alkalosis and elevation of the blood urea when he first came under our care on the sixth postoperative day. This was corrected by the infusion of increased amounts of salt and water, but the peak of the aspirate curve was not reached until the eighth or ninth day.

*She later volunteered the comment that she at first thought the tube had passed into his trachea, so marked was the initial gurgling of gas through it.

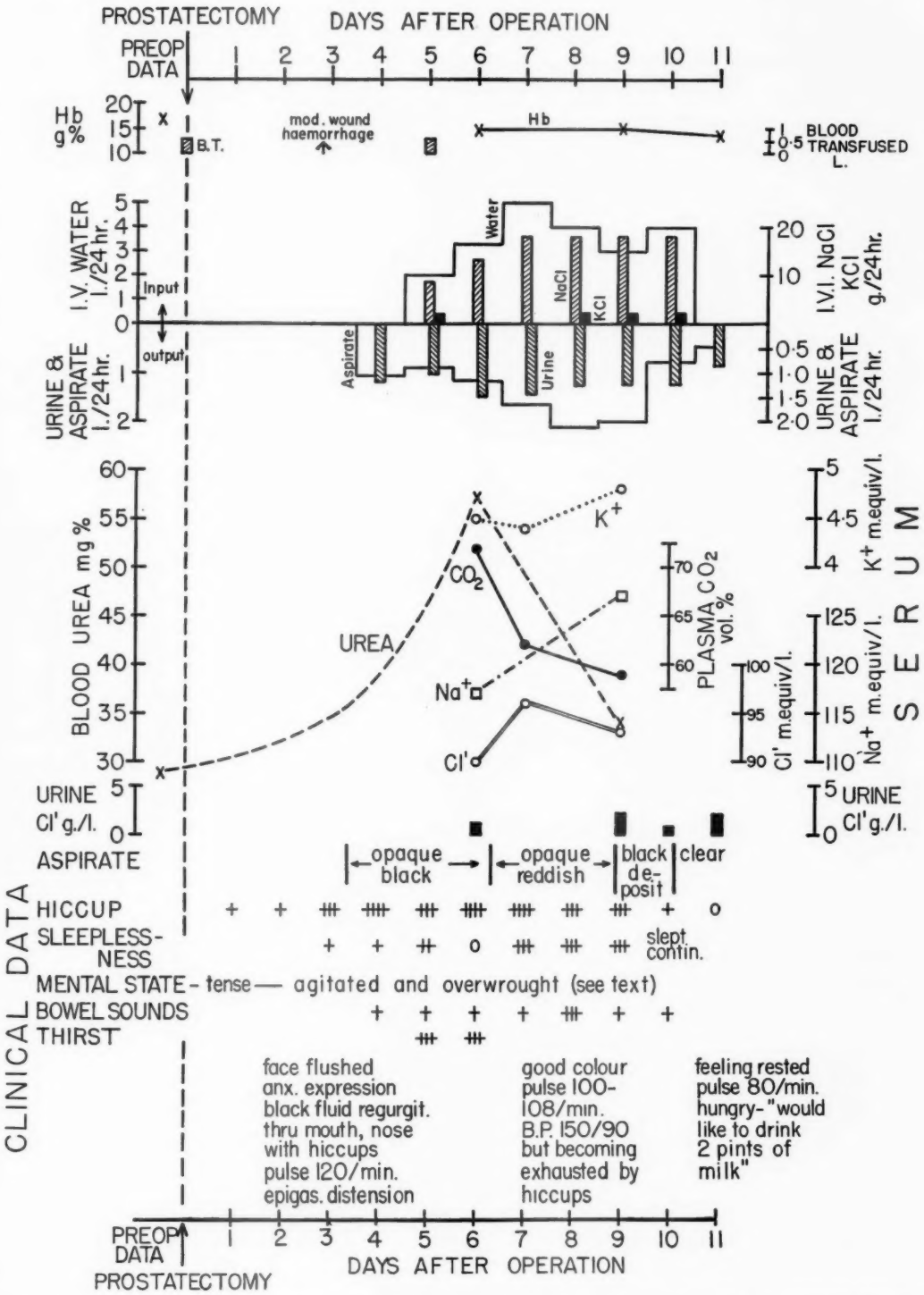

Fig. 5.—Acute hemorrhagic gastrorrhea following prostatectomy (Case 3). Heavy blood-staining of the aspirate, distressing hiccup, and sleepless ness were outstanding features. The patient presented beginning alkalosis and kidney failure when first seen. Over a 4-day period, 16 L. of water and 72 Gm. of sodium chloride were given intravenously.

Hiccup was intractable and prevented sleep. Relief was sought by numerous palliatives without effect but it was correctly predicted that as soon as the aspirate cleared his hiccup would go.

He was a tense, apprehensive person and even before the operation he had slept badly. During the gastrorrhea he slept for very short intervals only. In one 24-hour period, for example, he was given parenterally phenobarbital 9 gr., Pethidine 400 mg., and paraldehyde 12.5 c.c. and yet slept little. He has since told us that at this stage he felt his "last days had come." He had "lost all desire to live and felt wretched and hopeless."

The volume of the aspirate and his hiccup varied with his mental state. When he was agitated and slept poorly, his hiccup worsened and the aspirate volume increased. For example on the seventh and ninth postoperative nights he slept badly and the corresponding 6 P.M. to 6 A.M. aspirate volumes were 1,200 c.c. and 1,680 c.c., respectively. But during the sixth night, when he slept soundly, only 600 c.c. drained.

A feature of special interest was the audibility of bowel sounds during the most severe phase of the gastrorrhea. In fact, on the eighth postoperative day, they were clearly audible at the bedside without a stethoscope. He was given an enema with a good melena result.*

Finally, when on the tenth day the upset subsided, it did so rapidly. The volume and character of the aspirate reverted to normal. Hiccup passed off; on the eleventh postoperative day he slept almost continuously.

Comment. The characters of the aspirate and the associated clinical signs were similar to those in Case 2, but the disorder was much more severe and prolonged. Special features were the profuse blood-staining of the aspirate, the audibility of bowel sounds throughout the peak of the process, and the persistence of gastrorrhea well after an adequate fluid and electrolyte balance had been restored.

DISCUSSION

It is clear that the volume of material aspirated through an indwelling tube must be a function of that secreted by the related segment of the digestive tract. It will be smaller when the secretions are propelled quickly away from the tube tip by active peristalsis or reabsorbed into a healthy enterohepatic circulation.

We propose to consider only three disorders which, if unrelieved, lead to rapid dilatation of the stomach: (1) acute intestinal obstruction; (2) paralytic ileus, the bulk of all digestive secretions is poured into the stomach and duodenum and, in ileus, these and swallowed air, food, and drinks cannot be moved on and are not absorbed; and (3) acute hemorrhagic gastrorrhea, in which gastric distention may follow the vast outpouring of gastric juice.

*The possibility of hemorrhage from a peptic ulcer was considered in this patient but rejected. In fact, the total blood loss in the aspirate could not have been very great or comparable to that in bleeding ulcer. On the one hand, transfusion was limited and must barely have covered other known losses. Thus, only two units of blood were given throughout, one (500 c.c.) at prostatectomy, the other (500 c.c.) on the fifth postoperative day, following moderate wound hemorrhage possibly brought on by hiccupping. On the other hand, gastric bleeding continued for six days. Nevertheless the blood hemoglobin level remained at 14 Gm. per cent throughout. Clearly hemoconcentration was the dominant factor, not hemorrhage.

We would stress but need not discuss mechanical obstruction of the intestine with damming up of contents when peristalsis weakens and the proximal loops dilate. Second, there is paralytic ileus which occurs usually in association with sepsis or low-grade peritonitis after operations. Paralytic dilatation affects the gastrointestinal tract over a variable extent and to different degrees. But its chief impact is seen in the gastroduodenal area where there is pooling of secretions and accumulation of all swallowed material. Very large volumes of aspirate may be recovered but there is no firm evidence that the gastroduodenal secretions are increased in amount in paralytic ileus. The aspirated material is mixed in character, being bile-stained, greenish or brown and is foul-smelling.

It is clear that the expression, "acute dilatation of the stomach," has been widely used to describe conditions of gastroduodenal ileus (Johnson and Rabinowitch,[12] 1930; Slocumb,[13] 1927; Dragstedt,[14] 1952; Gold,[15] 1952) and even gastroduodenojejunal ileus (Grundy,[16] 1928; Solomon,[17] 1955). Thus Dragstedt, to whom we are indebted for careful post-mortem studies (Dragstedt and Dragstedt,[18] 1922; Dragstedt and his co-workers,[19] 1931), states that in most of his cases in which an examination was made the fluid from the stomach contained very little or no free hydrochloric acid and practically always contained bile. Evidently mixed or pooled specimens were analyzed. Indeed, many of his patients developed varying degrees of acidosis and this could only be explained if the fluid lost from the circulation consisted predominantly of postpyloric secretions. Dragstedt postulates that "acute dilatation of the stomach" is due to vagal inhibition and sympathetic hypertonus resulting from abdominal visceral and somatic reflexes. Whatever the mechanism, it would appear preferable to use the terms gastroduodenal, or gastroduodenojejunal, ileus (depending on the extent of bowel involved) to describe such states of atony with passive pooling of ingesta, swallowed air, and all digestive secretions.

We suggest that acute hemorrhagic gastrorrhea is a clinicopathologic entity which should be separated from paralytic ileus in any of its forms. It is an active process involving intense hypersecretion by the gastric mucosa. All the findings agree with this. Instead of the usual postoperative inhibition of secretion there is gastrorrhea.

The increased aspirate is not due to a failure of propulsion, with consequent pooling, because, as it develops, there is a switch to a purely gastric pattern in the biochemical analysis. It is almost odorless not feculent, and black not bile-stained or brownish.

According to Wolf and Wolff[20] (1944), secretory hyperfunction of the stomach is always accompanied by hyperemia. Their visual observations revealed that in states of marked hyperfunction the gastric mucosa became engorged, its folds being thick, red, and succulent. Stroking with dry gauze resulted in erosions and frequently minute hemorrhages occurred spontaneously following strong contraction of the stomach wall. Contraction of the engorged and hyperfunctioning stomach similarly caused abdominal discomfort and pain.

The aspirate findings in the present cases are clearly consistent with the proposition that intense gastric hypersecretion was associated with extreme engorgement of the mucosa and oozing of blood, this blood being in turn rapidly converted into acid hematin products and deposited on the excess mucus also being secreted. The symptom, hiccup, is well known to occur in association with extreme gastric irritation.[21, 22] The inaudibility of bowel sounds in Case 2 and their easy audibility in Case 3 indicate that the gastric upset may or may not be associated with poorly contracting intestines.

We may thus define acute hemorrhagic gastrorrhea as a grossly abnormal pouring out of secretions by the stomach, occurring after traumas, including operations not necessarily involving the peritoneal cavity, and associated with general malaise, wakefulness, upper abdominal distention and discomfort, hiccup, and rapidly progressive hypochloremic alkalosis. Its pathogenesis is unknown but vagal inhibition cannot be a factor. Further elucidation of its mechanism and its correct management demand that it be differentiated from simple postoperative ileus.

SUMMARY

1. The mean volume of the postoperative gastric aspirate in fasting patients recovering normally from general surgical operations reached a level of approximately 600 c.c. per 24 hours after five days but it is reduced to about one half of this volume in the first 24 to 48 hours.

2. By differential drainage of gastric, duodenal, and biliary secretions it can be shown that gastric contents account for most of this short-tube aspirate. The distinctive physical and biochemical patterns of separated gastric, duodenal, and biliary secretions have also been determined.

3. These three patterns can be used to interpret the biochemical findings in aspirate samples and their chief site of origin, as illustrated in a case of gastric resection.

4. The description, acute hemorrhagic gastrorrhea, is suggested for the postoperative complication characterized by enormous outpouring of blood-stained gastric juice, associated with malaise, hiccup, and hypochloremic alkalosis. Illustrative cases are cited. It is but one cause of acute gastric dilatation.

5. Acute hemorrhagic gastrorrhea can and should be distinguished from paralytic ileus with pooling of ingesta, swallowed air and all the gastroduodenal secretions. In the latter the aspirate is foul-smelling, more nearly neutral in reaction and is bilious, not blood-stained.

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THE USE OF I^{131}-LABELED ALBUMIN IN THE DIAGNOSIS OF PANCREATIC DISEASE

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THE diagnosis of pancreatic disease constitutes one of the major unsolved problems in clinical and laboratory medicine. Renewed clinical interest and laboratory investigation followed the introduction of serum enzyme determinations in acute pancreatic disease and have made possible great strides in the understanding and management of these conditions. A similar situation does not exist in subacute and chronic pancreatic disturbances. Simple reliable methods for the demonstration of pancreatic insufficiency are rare.

Recently Lavik, Chinn, and co-workers[1, 2] have introduced a test for pancreatic insufficiency which utilized a meal of I^{131}-labeled protein. That an individual's ability to digest and absorb such a protein is a measure of pancreatic function has been well established by the original authors and more recently by Shingleton and his associates[3] in preliminary animal and human studies. The reader is referred to these excellent articles for the experimental background of this test. The present study is an attempt to evaluate the sensitivity and practical value of this test in the study of patients with various forms of pancreatic disease.

A simple, reliable, and sensitive test of pancreatic insufficiency would permit not only earlier and accurate diagnosis of pancreatic carcinoma and benign pancreatic conditions, but also would provide a means of evaluating the efficacy of medical as well as surgical therapy for these states. The preoperative detection of pancreatic duct obstruction in cases of obstructive jaundice would alert the surgical team to the more formidable task ahead. In patients with chronic diarrheas and steatorrheas, the demonstration of pancreatic insufficiency renders therapy more accurate and diagnosis more exact. The degree of pancreatic insufficiency created or relieved by recent surgical procedures such as sphincterotomy, subtotal pancreatectomy, and retrograde pancreaticoenterostomy could be determined. In addition, the relatively more common conditions of acute and relapsing pancreatitis might be detected some time after serum enzyme levels had returned to normal.

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METHODS

The test employed in the present study has been described elsewhere.[1, 2, 3] It utilizes a meal of pure gelatin (0.5 Gm. per Kg.) to which is added 100 μc of I^{131}-labeled human serum albumin. In addition, 200 c.c. of distilled water as a diluent and a small amount of chocolate flavor for palatability are added. The meal is administered following a 12-hour fast and a 72-hour period of thyroid blockage with Lugol's solution. Intravenous blood samples are drawn in heparinized tubes at hourly intervals and were analyzed in a well-type scintillation counter for radioactivity. Whole blood volume was either measured by means of I^{131} human serum albumin dilution techniques or assumed to be 80 c.c. per kilogram in individuals without significant anemia or evidence of reduced blood volume. Results are expressed as the percentage of ingested isotope present in the whole blood volume at a given hourly interval. The test is as simple to perform and no less disturbing to the patient than a glucose tolerance test. The time required is only three to four hours and an experienced isotope technician can carry out twenty or more tests in a morning.

Previous studies[1, 2] have shown that less than 5 per cent of the ingested I^{131} is released from the albumin molecule by means other than protein breakdown. Studies[2] utilizing a stool collection technique have correlated well with the blood concentrations in reflecting the percentage of isotope which is absorbed as compared with that amount excreted in the fecal residue.

The patients studied were from the wards of the Cook County Hospital and represent a wide variety of benign and malignant pancreatic diseases. In addition to routine control subjects free of gastrointestinal disturbances, special control subjects were chosen to investigate the relative importance of factors of gastrointestinal mobility and altered intestinal absorption.

RESULTS

The results are best summarized by a review of the graphs. In Fig. 1, it is readily apparent that the normal individual will show a peak concentration of isotope in the blood at two or three hours with a gradual return to the isotope-free state. In addition, the normal individual's peak level may vary from 10 per cent to 22 per cent but in no instance did the normal controls show peak concentrations below 10 per cent of the isotope ingested. Similarly, a group of special controls with nonpancreatic diarrhea including regional ileitis (3), amoebiasis (2), acute nonspecific gastroenteritis (5), and nontropical sprue (2) were generally at the lower limits of normal, but at no time fell below 10 per cent at the peak concentration. Four patients with moderate pyloric obstruction were studied and reached their peak concentrations somewhat slower than normal controls, but concentration invariably rose above 10 per cent of ingested isotope within the first four hours.

In contrast, 9 cases of pancreatic insufficiency showed much flatter curves with peak levels above 5 per cent in only one instance and the remainder of isotope concentrations generally below 4 per cent. These cases represent postoperative pancreatectomy (1), pancreatic calcification associated with diabetes, creatorrhea and steatorrhea, plus a history of recurrent episodes of acute pancreatitis (5), and autopsy proved chronic pancreatitis in which multiple sections of the pancreas failed to demonstrate morphologically normal pancreatic parenchyma (3). In all of these cases, typical pancreatic diarrhea was present and 2 of the 3 were diabetic. At some time in the course of their hospital stay, diarrhea was a problem requiring definitive therapy, but diarrhea was not constant in all, and repetition of the test during episodes when patients were free of diarrhea gave no significant changes from the earlier tests.

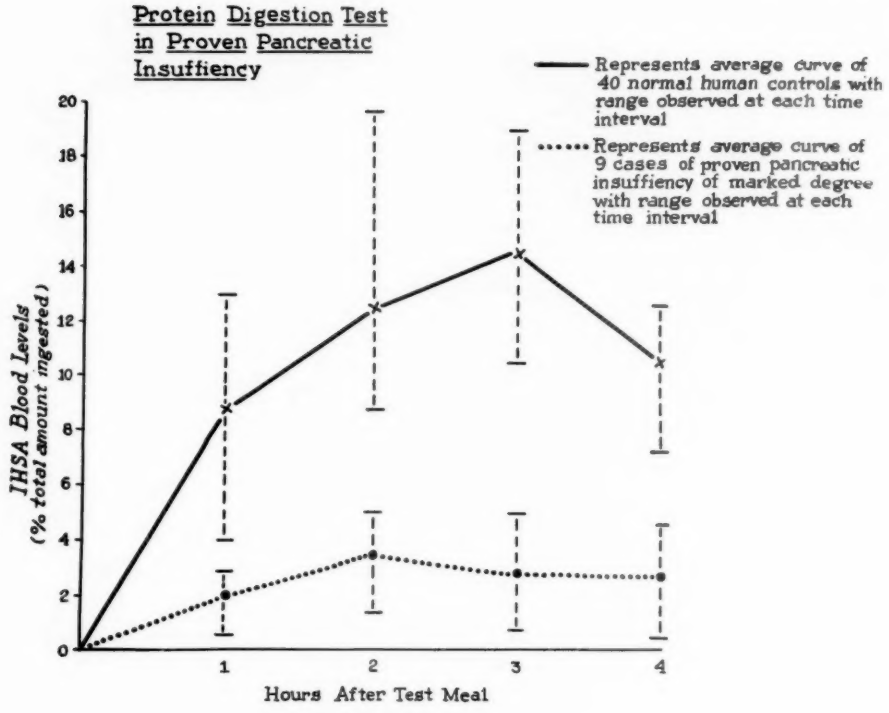
Protein Digestion Test
in Proven Pancreatic
Insuffiency
Represents average curve of 40 normal human controls with range observed at each time interval
Represents average curve of 9 cases of proven pancreatic insuffiency of marked degree with range observed at each time interval
IHSA Blood Levels
(% total amount ingested)
0
2
4
6
8
10
12
14
16
18
20
1
2
3
4
Hours After Test Meal

Fig. 1.

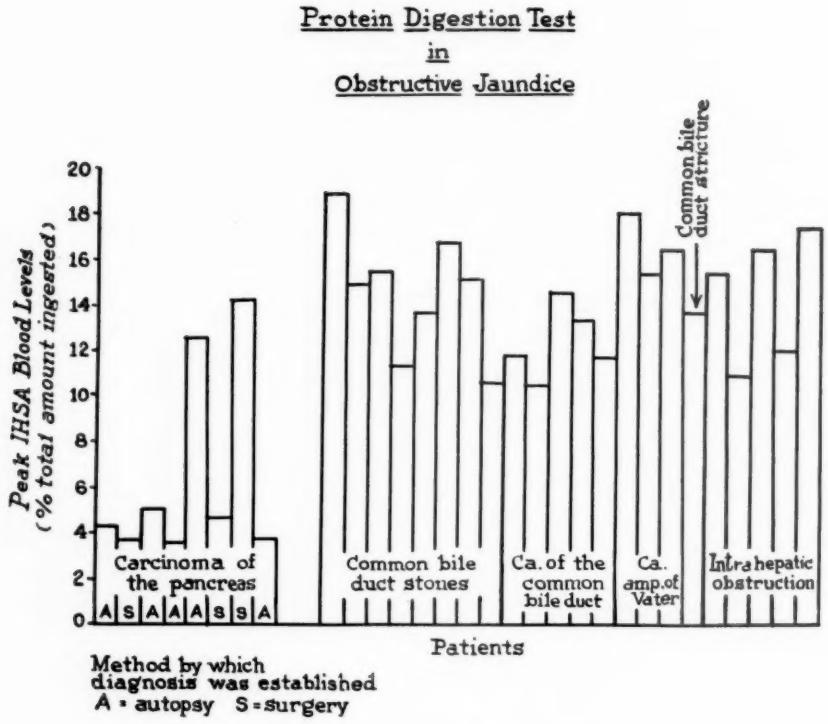
Protein Digestion Test
in
Obstructive Jaundice
Peak IHSA Blood Levels
(% total amount ingested)
0
2
4
6
8
10
12
14
16
18
20
Common bile duct stricture
Carcinoma of the pancreas
A S A A A S S A
Common bile duct stones
Ca. of the common bile duct
Ca. amp. of Vater
Intrahepatic obstruction
Patients
Method by which diagnosis was established
A = autopsy S = surgery

Fig. 2.

Thirty cases of obstructive jaundice were studied and are illustrated in Fig. 2. In 8 of these cases, surgery or autopsy demonstrated the mechanism of jaundice to be a carcinoma of the pancreas obstructing the common bile duct. In the remainder, the mechanism of jaundice was extrapancreatic in origin and included carcinoma of the common bile duct (5), common bile duct stones (8), or strictures (1), carcinoma of the ampulla of Vater (3), and hepatic parenchymal disturbances (5). A review of these results shows that in 6 of the 8 cases of obstructive jaundice due to carcinoma of the head of the pancreas, there was definite evidence of pancreatic insufficiency. In the remaining 2 cases, protein digestion was similar to that in normal individuals. In the 22 cases of nonpancreatic obstructive jaundice only one showed abnormal protein digestion preoperatively. This individual at operation had a stone impacted at the ampulla of Vater and a grossly normal pancreas. Postoperatively his protein digestion returned to normal and it is possible that the stone brought about a simultaneous obstruction of the common bile and pancreatic ducts.

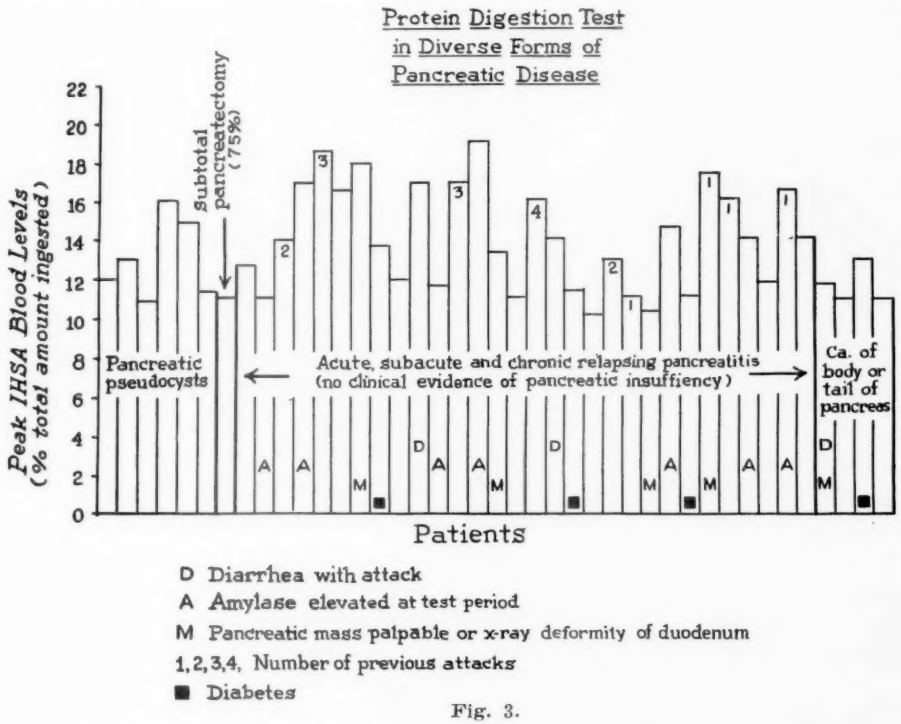
Protein Digestion Test
in Diverse Forms of
Pancreatic Disease
Peak IHSA Blood Levels
(% total amount ingested)
Subtotal pancreatectomy (75%)
Pancreatic pseudocysts
Acute, subacute and chronic relapsing pancreatitis
(no clinical evidence of pancreatic insuffiency)
Ca. of body or tail of pancreas
Patients
D Diarrhea with attack
A Amylase elevated at test period
M Pancreatic mass palpable or x-ray deformity of duodenum
1,2,3,4, Number of previous attacks
■ Diabetes

Fig. 3.

The finding of normal protein digestion in the 3 patients with carcinoma of the ampulla of Vater and obstructive jaundice is of interest and is best explained by postulating a common duct tissue origin of the tumor with pancreatic secretions reaching the intestine through a separate or accessory pancreatic duct.

The value of this test in the differential diagnosis of obstructive jaundice is readily apparent in that a flat curve indicates simultaneous pancreatic and common duct obstruction and is strongly suggestive of pancreatic carcinoma.

Studies carried out on patients with acute pancreatic disease and with localized disease of the pancreas are shown in Fig. 3. Significant alteration

from those of normal controls did not occur. Included in this group were patients with pancreatic pseudocyst (6), acute pancreatitis without evidence of pancreatic insufficiency (6), and carcinoma of the body and tail of the pancreas (4).

Several points should be stressed with regard to these patients. The 6 cases of pancreatic pseudocyst were clinically clear-cut and secondary to pancreatic trauma or acute pancreatitis. Their size varied from the smallest, which was the size of an orange, to the largest which contained over 6,000 c.c. of fluid. The finding of normal protein digestion in all is further evidence of the diagnostic difficulties attending this interesting condition.

In the 4 patients with carcinoma of the body and tail of the pancreas, repeat tests were possible later in the disease, but suggestive evidence of pancreatic insufficiency occurred in only one and in a near preterminal state. One of these patients was originally studied as a nonspecific diarrhea and demonstrated to have excellent protein digestion by the test and careful stool analysis. The diarrhea subsided prior to surgery and only late in the patient's progressive downhill course was it to recur in a different form characteristic of pancreatic insufficiency. This case no doubt illustrates the fact that the diarrhea seen early in pancreatic carcinoma is a reflex increase in gastrointestinal motility, rather than inadequate pancreatic digestion and absorption.

Three patients were studied before and after sphincterotomy without significant change in protein digestion. One of the patients continued to show her original curve of pancreatic insufficiency.

A single patient subjected to total pancreatectomy for carcinoma of the ampulla of Vater was converted from normal protein digestion to a flat abnormal curve postoperatively. The latter was almost completely corrected by vigorous oral administration of pancreatic granules.

Five patients with pancreatic calculi were studied and abnormal protein digestion was noted in 4 of the 5 although diarrhea was present clinically in only 2 of the 4 abnormal patients at the time of the examination.

DISCUSSION

Previous methods for the diagnosis of exocrine pancreatic dysfunction are both difficult to perform and to interpret. In the past emphasis has been placed on one of four different approaches to this problem:

1. The analysis of the fecal residue for evidences of incomplete fat or protein digestion.

2. Blood and urine enzyme determinations with or without the use of provocative drugs to stimulate pancreatic function.

3. Studies of the pancreatic secretion as obtained by duodenal intubation.

4. The investigation of carbohydrate metabolism for evidences of pancreatic islet cell insufficiency.

Each of these approaches has its advocates and one or all may be of value in the investigation of an individual case. Each has its individual limitations and shortcomings and all are limited by the very nature of the problem under discussion. When one takes into consideration the great functional reserve of

the pancreas and the established fact that as much as 95 per cent of the gland may be removed without a demonstrable laboratory deficit being created, this latter difficulty seems insurmountable.

Studies of the fecal residue require careful collection and preservation of the stool as well as laborious chemical analyses. In addition, defects of absorption and intestinal motility introduce factors which render difficult the final interpretation of results. Further, the patient with chronic pancreatic disease or pancreatic carcinoma frequently is unable to ingest the standard diet required because of the anorexia that so frequently accompanies these conditions.

Dreiling and Richman[4] have recently pointed out the inadequacies of the provocative blood enzyme determinations and emphasize the impossibility of interpreting the varied results usually obtained. The unstimulated serum and urine enzyme determinations are of value only during the acute episode of pancreatitis and are rarely helpful in cases of pancreatic carcinoma.

Duodenal drainage studies require the greatest amount of time and patience from the patient, doctor, and laboratory and, except as carried out by the same technicians in a well-standardized manner, give results which are far from reliable.

The demonstration of the presence of latent diabetes by means of glucose tolerance tests is felt by some to represent the single most important laboratory test available in the investigation of a patient suspected of chronic pancreatic disease. Its simplicity is indeed an excellent recommendation, but the frequent occurrence of latent diabetes in the general population limits its value as a definitive diagnostic tool.

A fifth approach to the problem might be identified by the term "pancreatic digestion tests," and is exemplified by the protein, fat, or starch meal. Tests of this sort are designed to measure indirectly the quality and quantity of exocrine pancreatic secretion by its effect upon an ingested meal of protein, fat, or starch. Following the meal, studies of the blood are undertaken to determine the presence and amount of the products of digestion as an index to the completeness of this process. In addition to their relative simplicity and minimal patient inconvenience, the digestion-type studies carried out in the first few hours after a meal reflect indirectly the digestive abilities of the upper gastrointestinal tract only, that is, primarily pancreatic, and less interference from the digestive action of the succus entericus is anticipated. This constitutes an improvement over the stool analysis type of study where defects of digestion on the basis of pancreatic insufficiency may be masked by the accelerated function of subpancreatic digestive processes. Certain limitations and special considerations exist for this type of testing also and render difficult the interpretation of a digestion-type test. Defects in absorption as encountered in intrinsic diseases of the small intestine may reject the products of pancreatic digestion and give low blood concentrations in the presence of normal pancreatic digestion. Similarly, alterations of gastrointestinal motility, as in pyloric obstruction (reduced), or simple gastroenteritis (increased), may affect the results obtained at any given time following a meal, independent of the effectiveness of pancreatic function. In our experience, with the exception of high-grade pyloric obstruction, little interference with the interpretations of results has arisen

because of the above-mentioned factors. Two patients with an intestinal absorptive defect for fat and carbohydrate of the type seen in sprue showed no evidence of impaired protein digestion and absorption with the test meal.

A review of the case material presented makes it readily apparent that localized pancreatic disease involving the duodenal portion of the pancreatic duct may give rise to total pancreatic insufficiency, but that extensive pancreatic destruction that spares the duct system and a small portion of functioning parenchyma may be unassociated with evidence of pancreatic exocrine or endocrine insufficiency.

The group of cases of localized pancreatic disease and those with diffuse pancreatic disease in an inactive state constitute the chief hurdle in pancreatic diagnosis. The present test has little to offer with regard to these cases except to rule out the presence of diffuse pancreatic destruction. In a case of a patient with carcinoma of the body of the pancreas mentioned earlier, who was tested three times over a period of six months, it was possible to demonstrate intermediate degrees of impaired protein digestion at a time when pancreatic destruction was incomplete but surgical attack was no longer feasible. In 2 of the cases of acute pancreatitis, diarrhea was a prominent clinical feature and the presence of normal protein digestion during this time tends to refute the existing opinion that the diarrhea of acute pancreatitis is the result of transient pancreatic insufficiency.

The finding of normal protein digestion in various stages of acute pancreatitis is in contrast with the results reported by Shingleton and co-workers.

The patients with diarrhea of undetermined origin constitute a group not uncommon on the wards of a large charity hospital. In these cases, chronic pancreatitis is frequently suspected yet rarely confirmed or eliminated from diagnostic consideration. We believe a normal protein digestion curve rules out pancreatic insufficiency as the cause of the diarrhea in as simple and reliable a manner as is now available. The following case history illustrates this point.

> W. J. entered the hospital with complaints of foul smelling diarrhea of seven weeks' duration. Past history revealed a long and excessive consumption of alcoholic beverages and recent upper abdominal pain. Routine x-ray and blood chemical studies including serum amylase and lipase determinations and fasting blood sugar were within normal limits and studies of fecal residue showed excessive amounts of undigested fat and muscle fibers. The patient was considered to have chronic pancreatitis with insufficiency and a protein meal using I^{131}-labeled albumin was administered. Results of this test revealed protein digestion within normal limits. Surgical exploration followed and revealed extensive regional enteritis of the lower jejunum and ileum.

In the patients with obstructive jaundice and evidence of pancreatic insufficiency as shown by flat protein digestion curves, the likelihood of pancreatic carcinoma is statistically overwhelming. Since the rare possibility of a common duct stone producing simultaneous pancreatic and common duct obstruction cannot be denied, these patients must be surgically explored. However, the preoperative preparation is frequently more rational with a working diagnosis tentatively established. Case 2 is illustrative.

> A. K. was a 65-year-old white man who entered Cook County Hospital with a seven weeks' history of jaundice, 30-pound weight loss, clay-colored stools, and

pruritus. Food intolerances and abdominal pain were denied in the past or on admission. Physical examination revealed marked jaundice and a readily palpable nontender globular mass in the right upper quadrant which moved with respirations. Laboratory studies revealed an icterus index of 120 and alkaline phosphatase of 30 units and normal serum enzyme levels and hepatic parenchymal functions. The patient was considered to be a clear-cut case of advanced carcinoma of the head of the pancreas with a Courvoisiers' gall bladder and because of his poor general condition was scheduled for a simple cholecystojejunostomy under local anesthesia. A protein digestion study revealed no evidence of pancreatic insufficiency. Further preoperative management was instituted to prepare the patient for a more extensive surgical procedure and subsequent exploration revealed a normal pancreas, markedly dilated gall bladder and common bile duct, and numerous impacted stones in the intrapancreatic portion of the common bile duct.

SUMMARY AND CONCLUSIONS

1. Advances in the diagnosis of subacute and chronic pancreatitis and pancreatic carcinoma have failed to keep pace with recent improvements in diagnosis of acute pancreatitis.

2. Most of the laboratory methods of value in the diagnosis of pancreatic insufficiency are laborious and unreliable and restricted to large medical centers with extensive laboratory facilities and unusually cooperative patients.

3. The isotope-labeled protein digestion tests described first by Lavik, Chinn, and co-workers[1, 2] offers a simple accurate method of confirming the presence of pancreatic insufficiency with the facilities of the most simple isotope laboratory the only requirement.

4. The test is of particular diagnostic value in the study of patients with diarrhea of undetermined origin and cases of obstructive jaundice. It is a simple means of confirming the diagnosis of pancreatic insufficiency.

5. There are no reliable laboratory methods available for the diagnosis of localized disease unassociated with pancreatic duct obstruction.

ADDENDUM

Since preparation of this manuscript, 21 additional pancreatic function tests have been carried out using the same technique. Ten of these having normal absorption curves included the following clinical diagnoses: acute pancreatitis (4 cases) and one case each of chronic pancreatitis, carcinoma of the body of the pancreas, common duct stone, gastric ulcer, pseudocyst of the pancreas, and ulcerative colitis. Eleven additional abnormal absorption curves were found having the following clinical diagnoses: calcified pancreas (2 cases), pseudocyst of the pancreas (2 cases), atresia of the common bile duct (2 cases), and one case each of diabetes mellitus with diarrhea, steatorrhea, carcinoma of the ampulla of Vater, carcinoma of the head of the pancreas, and pancreatic fistula.

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BILIARY DRAINAGE

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THE postoperative problems of biliary tract surgery are still largely unsolved. Reports of the postcholecystectomy syndrome and the unsatisfactory results following common duct surgery constantly appear in the surgical literature.[3, 8, 13 14, 20-22, 28, 38, 40, 41, 44, 47, 54-56] Since 1929, when Mirizzi[36] introduced the use of contrast media to study the common duct, attention has been directed chiefly toward the development of new techniques for better diagnosis. These include operative and postoperative cholangiography, intravenous cholangiography, manometric studies (with and without contrast media), endoscopy of the bile ducts, and stone detectors. Such techniques have been helpful in discovering pathologic conditions in the biliary ducts and in evaluating the results of surgical treatment.

Sharper definitions should be developed in this somewhat clouded field of the postcholecystectomy and postcholedochotomy syndrome. We should reexamine our surgical approaches to determine if we, as surgeons, may be responsible for some of these unpleasant sequelae.

In the recent literature, Sandweiss and Fulton[48] report moderate to severe symptoms in 10 to 25 per cent of the patients who have had cholecystectomies for cholelithiasis and in 50 per cent when this procedure was carried out for the noncalculous gall bladder. Using Cholografin, they found normal cholangiograms in only 36 per cent of 94 patients suffering from postcholecystectomy symptoms. McClenahan and co-workers[30] studied the postcholecystectomy syndrome in 121 patients. They found major abnormalities in the common duct in 40 (33 per cent) and pancreatitis in 7 (5.8 per cent).

These two studies were made on patients in whom no corrective procedure had been attempted on the common duct. After attempts to correct common duct pathology, the following discouraging results have been noted.

Preston and Alden[40] analyzed 74 postoperative cholangiograms made through an indwelling T-tube after common bile duct surgery and found normal ducts in 56.7 per cent, stones in the common duct in 24.3 per cent, and partial or complete obstruction of the distal one third of the common duct in the remaining 19 per cent.

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Starr,[54] after choledochotomies performed on 92 out of 384 patients undergoing biliary surgery, concluded that "the T tube was an imperfect solution to the cure of the different diseases of the common bile ducts."

The postbiliary surgery syndrome may be related to the following more specific conditions: (1) hypertonus of the lower third of the common duct; (2) stones in the common duct and cystic stump duct syndrome; (3) stricture of the common duct; (4) stenosis of the papilla of Vater; (5) sclerosis of the papilla; (6) hypertrophy of the papilla; (7) benign tumors of the papilla; (8) choledochitis; and (9) pancreatitis.

Most of these may be related to what Leon Gimenez[28] calls "biliary hypertension." Infection may be expected to develop whenever there is any element of obstruction to the free flow of bile. The trauma produced by surgical attack on the gall bladder or common bile duct may be sufficient to produce reflex spasm of the muscular structures associated with the distal third of the common duct. In 1927, Del Valle[57] referred to a condition called "fibrous odditis" which he found in 10 per cent of his patients after cholecystectomy. He explained it as being secondary to a mild but chronic cholangitis which induced spasm of the sphincter of Oddi. Intractable stenosis and sclerosis of the sphincter, ampulla, and papilla result from the association of long-standing infection and spasm.[6] Cattell[11] has expressed these same views on the etiology of fibrosis of the sphincter of Oddi. It is suggested that sclerosing choledochitis and chronic pancreatitis are later sequelae of a progression of the above chain of events. Diffuse stricture of the common duct may be a late and result of inadequate bile drainage, as reported by Baron and Yamashito.[4] As early as 1918, Archibald[2] felt that hypertension in the bile ducts was the chief cause of pancreatitis.

The sphincter mechanism at the termination of the common duct is complex and poorly understood. In 1923, Westphal[62] described two parts of the sphincter of Oddi—a proximal part surrounding the antrum, and a distal group of fibers surrounding the ampulla. Lueth[29] agrees with Westphal. In 1937, Boyden[7] described three parts to the sphincter—the sphincter choledochus, extending proximally from the junction of the choledochus and the ampulla and considered the most powerful part of the mechanism; the sphincter pancreaticus, encircling the lower end of the main pancreatic duct; and the musculus proprius ampullae, which he considered to be weak and undergoing retrogression. Some investigators deny the presence of any sphincter muscle. The question arises as to whether the muscle fibers described are independent structures or whether they represent extensions of the intrinsic duodenal muscularis.

Kapandji,[24] by radiomanometric studies, demonstrated that biliary hypertension may result from spasm of the duodenal musculature without associated inflammatory disease of the sphincter of Oddi or the papilla of Vater. He calls this segment of the common duct traversing the duodenum the duodeno-Oddi segment. Hypertension in the bile duct can be induced in a patient after sphincterotomy by the administration of morphine. Normally, the pancreatic duct pressure is higher than the common duct pressure.[39] Organic or functional disturbance in this segment of the common duct, which causes a rise in the

biliary pressure, may disrupt this relationship between the biliary and pancreatic pressures, first causing stagnation of the pancreatic secretion and, eventually, regurgitation of bile into the pancreatic duct. A 60 per cent incidence of sepsis following obstruction of the common bile duct can be expected.[53] This infection and biliary hypertension are probably of great etiologic significance in chronic pancreatitis, particularly in that part of the pancreas adjacent to the duct. The inconsistent results of sphincterotomy in the treatment of chronic relapsing pancreatitis are understandable, since more than the papilla and distal centimeter of the duct may be involved.

It is suggested that routine use of the short-arm T-tube is unwise and may perhaps be responsible for the production or aggravation of biliary surgery sequelae. As previously mentioned, even without initial infection, the inflammatory response to surgery of the bile ducts can induce spasm of the sphincter mechanism and duodenum and increase intraductal pressure. The reflux of bile from the common duct up through the T-tube does not eliminate the factor of stagnation.

Undoubtedly, the greatest improvement in the T-tube, from the point of view of its use as a therapeutic agent, is the introduction by Catell,[25] in 1946, of the long-arm variety which traverses the entire distal common duct. Even the use of this T-tube, however, is still far from ideal. The use of T-tubes offers many objectionable features.

1. Bile leakage from the choledochostomy opening at the time of insertion or removal of T-tubes which may result in varying degrees of bile peritonitis, with an increase in the reflex spasm of the duodenal wall and the sphincter mechanism. This, in turn, interferes with the healing of the incision in the common duct, and may result in a fistula. Infection and later strieturing of the duct may occur with the development of firm pericholedochol adhesions and perivisceritis.

2. Leukocytic infiltration and fibrosis in the common duct wall are often caused by irritation from the rubber in the T-tube (the majority of T-tubes now in use are made of rubber). In an experimental study of end-to-end anastomoses on the common ducts of dogs, Lary and Sheibe[26] found that when a rubber T-tube was used, stricture occurred four times as frequently as when none was used.

3. Hemorrhage from the common duct may be caused by an indwelling T-tube.[10, 27, 43]

4. Disruption of the enterohepatic circulatory cycle resulting from the syphoning away of all of the liver's secretions. Bile normally mixes with the food and its secretion is in turn stimulated by the reabsorption of bile salts from the gut. If the vertical limb of the short-arm T-tube is left open, the pressure in the common duct almost never rises sufficiently to overcome the tonus of the sphincter of Oddi.

5. Reoperation may be necessary to recover retained fragments of T-tubes broken at the time of removal.

6. Spillage of bile within the abdomen may be caused by the dislodging of the T-tube after insertion.

7. The patient is inconvenienced and hospitalization prolonged.

8. The T-tube is unsatisfactory for postoperative study, although this has been given as one of the chief reasons for its use. Postoperative cholangiographic studies have not been as helpful in practice as was originally hoped. Ideally, a complete and accurate study of the common bile duct should be accomplished during the laparotomy by clinical inspection, palpation, and cholangiography. Waiting until the patient is convalescing from surgery to discover a correctible defect is of questionable service to him.

We believe that the association of manometric readings with multiple radiographic views of the biliary tract can greatly improve the accuracy of the diagnostic technique.[1] The persistence of symptoms, postoperatively, may be investigated by the intravenous cholangiographic technique. Glenn[19] reports satisfactory visualization of the common duct by intravenous cholangiography in 86.8 per cent of the 121 postcholecystectomy patients studied. Sandweiss and Fulton[48] report good results in 94 per cent of 100 patients observed. When compared with the findings of Kantor, Evans, and Glenn[23] who found unsatisfactory results in 34 per cent of postoperative T-tube cholangiography, this reason for inserting a T-tube loses some of its rationale.

9. The loss of one of the major neutralizing agents of gastric acidity by diversion of bile from the duodenum may result in the development of duodenal ulcers. Puestow[42] recognized this problem in Roux Y choledochojejunostomy.

In addition to these major objections to the use of the T-tube there are several lesser technical pitfalls,[53] such as: (1) the tube is occasionally inserted between the mucosa and muscularis of the common duct in which case the duct will be obstructed and no bile will enter the T-tube; (2) if either arm of the T-tube is too short, it may accidentally slip out of the duct; (3) the proximal arm may be slipped into the cystic duct stump, into the right or left hepatic ducts, or against the carina at their bifurcation; (4) the distal arm may be slipped into a recess or pocket in the common duct; (5) either arm may be doubled up on itself; (6) in case of an oblique incision in the common duct, the approximating sutures may be improperly placed, thus permitting copious escape of bile; and (7) improper postoperative care of the T-tube by ward personnel may result in reflux of the drainage bile back into the biliary system, loss of an excessive amount of bile, or the development of excess pressure in the T-tube.

In an attempt to eliminate some of the complications of T-tube drainage, a method of internal biliary drainage has been devised and tested in laboratory animals. To avoid the above complications, an internally placed tube was designed to: (1) provide complete decompression of the common duct; (2) insure passage of the bile into the duodenum; (3) obviate biliary fistula and perivisceritis; (4) preserve the sphincter mechanism of the common bile duct; (5) eliminate the use of rubber within the bile duct; and (6) automatically pass into the duodenum after a period of time.

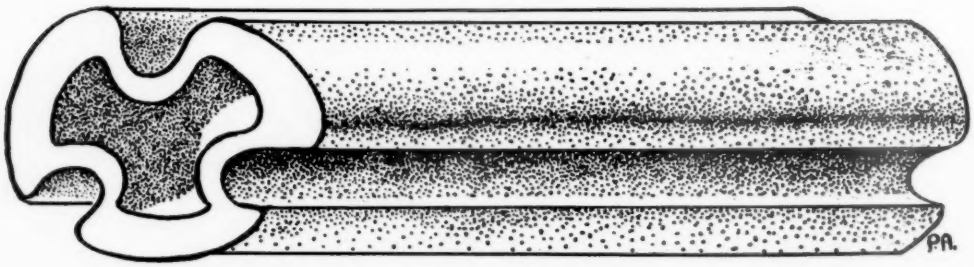

Fig. 1*A*.—Detail drawing of Polyvinyl tube.

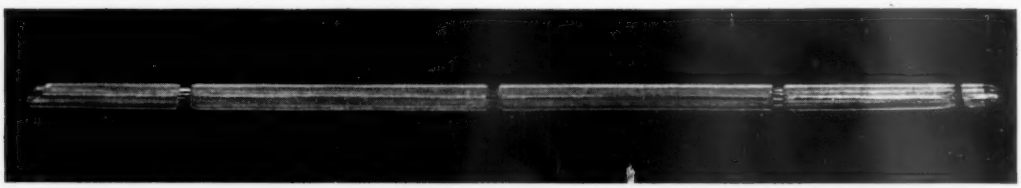

Fig. 1*B*.—The Polyvinyl tube with longitudinal grooves and tantalum bands used in the internal biliary drainage experiment.

Fig. 2.—Postoperative roentgenogram of grooved polyvinyl tube in place.

METHOD

The plastic drainage tube was constructed of Polyvinyl, which in contrast to polyethylene remains supple when in contact with bile.* Three longitudinal grooves were produced in the outer surface to permit bile flow around as well as through the tube (Fig. 1*A*). It was marked for x-ray visualization by three bands of tantalum recessed into the surface of the tube. The length was varied to permit 2 cm. to remain proximal to the choledochotomy site and 3 cm. to project into the duodenal lumen (Fig. 1*B*). The diameter of the tube was varied so that it never fitted tightly into the lumen of the duct. The location of the tubes was followed by occasional x-ray films (Fig. 2), and careful search of the stools.

It may be anticipated, on the basis of several studies by McWorther,[34] in 1929, and Douglass and his co-workers,[16] in 1950, that choledochotomy incisions in dogs heal with fibrotic and inflammatory reaction, since the dogs' bile is practically universally infected. This reaction can be modified by diverting the bile proximal to the site of surgery, but in our case this would have interfered with the purpose of our experiment.

TABLE I. RESULTS OBTAINED IN 14 MONGREL DOGS AFTER USING INTERNAL BILIARY DRAINAGE

DOG	TIME TO PASS TUBE (DAYS)	POSTOPERATIVE LEAKAGE OR BILE PERITONITIS	DEATHS
1	9	0	0
2	30	0	0
3	9	0	0
4	20	0	0
5	?	0	0
6	14	0	0
7	?	0	0
8	7	0	0
9	?	0	0
10	6	0	0
11	13	0	0
12	13	0	0
13	?	0	0
14	7	0	0
	Average 12.8		

RESULTS

Fourteen mongrel dogs of an average weight of 14.5 Kg. were used. Nembutal anesthesia was given. Exposure was produced through a paramedian incision and traction was applied to the duodenum to bring the common duct into view. The hepatoduodenal ligament was incised and the common duct cleared sufficiently to permit a small longitudinal incision. Through this incision, the Polyvinyl drainage tube was inserted with the distal portion extending through the papilla and 3 cm. into the duodenum. The proximal end of the tube was anchored with a 5-0 silk suture to the mucosa of the common duct above the choledochotomy site and the hepatoduodenal ligament closed over the duct (Fig. 3). Neither drainage of the abdominal cavity nor antibiotics were used in any of the 14 dogs.

The tubes were passed spontaneously in an average time of 12.8 days (Table I). In 4 of the dogs, the exact time of passage was not known. These 4 were reopened at 21, 63, 69, and 71 days, and the tubes were no longer present.

*Early tubes prepared by the Biophysical Instrumentation Department of the Walter Reed Army Institute of Research, and later furnished through the courtesy of the American Cystoscope Makers, Inc., of New York, N. Y.

The time between insertion and passage of the tube varied between 6 and 30 days and those tubes fitting the lumen of the duct most snugly remained the longest. The tube should not fit tightly in the duct. The common duct of the dog averages only 3 mm. in diameter making it difficult to use the tube which we have described.

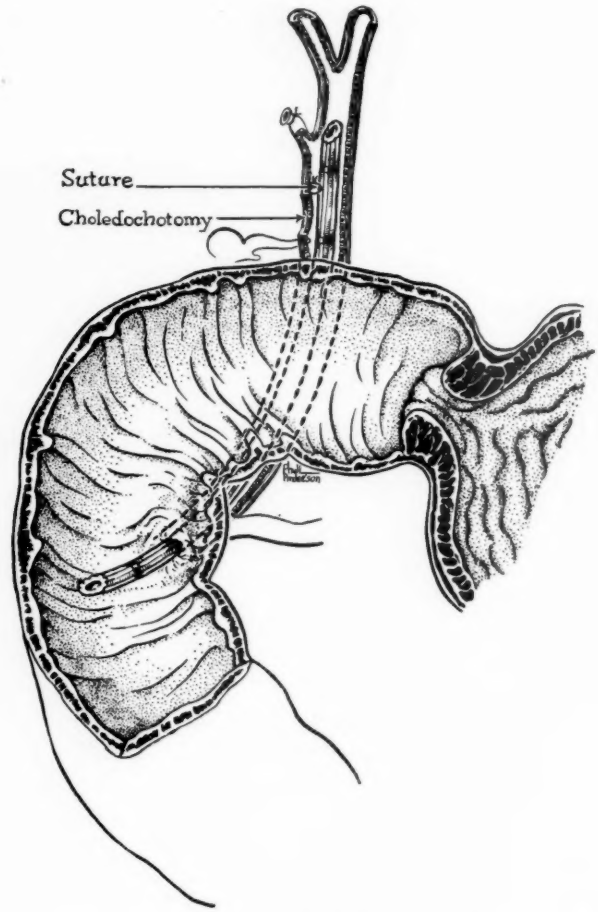

Fig. 3.—The internal biliary drainage tube in place.

In the ten Polyvinyl tubes recovered, the silk used to suture them to the mucosa was found intact and attached to the tube. Apparently the tube passed after the silk suture produced necrosis of the fragment of mucosa through which it was placed. The expulsion of the tube depends upon the length of time it takes for necrosis to free the anchoring suture and on the peristaltic action of the common duct and duodenum. In a later series of dogs in which the drainage tube was attached to the common duct by a suture through the entire duct wall, the average time of passage was 29 days.

There was no bile leakage, bile peritonitis, or postoperative death in this group despite the fact that no drains or antibiotics were used. None of the dogs developed any evidence of jaundice.

All dogs were submitted to reoperation and the segment of duct containing the previous choledochotomy site was resected for histopathologic study. These segments were removed at intervals varying from 7 to 71 days.

At the time of reoperation, adhesions were few and these were found only between the hepatoduodenal ligament and the adjacent inferior surface of the liver. In some of the dogs there were no adhesions.

Macroscopically, the ducts were somewhat dilated and the walls were thickened. Microscopically, inflammatory reaction was prominent. This type of healing was expected.

DISCUSSION

There is a justified fear among surgeons regarding the use of "lost" tubes in the common duct. These have almost always been used in reconstructive surgery of the bile ducts. Many ingenious methods have been devised to maintain these tubes in place to prevent stricture development at the site of anastomosis. This has been particularly true when tubes have been used to bridge defects and then wrapped in any available adjacent tissue. The majority of these tubes do not traverse the distal common duct into the duodenum.

There have been objections to the use of tubes that extend into the duodenum from the common duct, because of the fear of developing an ascending cholangitis. We feel that the establishment of free bile flow is the most important factor in the treatment or prophylaxis of biliary tract infection. The results of choledochoduodenostomy and of the use of the long-arm T-tube support this view. The administration of antibiotics following common duct surgery seems advisable, since a 60 per cent incidence of infection may be expected if obstruction develops.

Objections have arisen over the use of the long-arm T-tube because of the possibility of inducing pancreatitis. After using this tube for several years in a large number of patients, however, Cattell[12] reports only 2 cases of pancreatitis which might possibly have been related to use of the tube. The tube described seems to us theoretically less objectionable because of its longitudinal grooves and small diameter.

In a paper now in preparation,[49] we will report the satisfactory use of the tube for internal biliary drainage and splinting in 40 dogs submitted to common duct grafting. In published work on experimental bile duct repairs on dogs, early postoperative death, leakage at the anastomosis site, and bile peritonitis have accounted for 14 to 57 per cent of the complications. This method of biliary drainage minimizes perivisceritis, loss of bile salts, fluid, and electrolytes, as well as stricture formation, postoperative spasm of the duodeno-Oddi sphincter mechanism, and consequent biliary hypertension. It should also assist in preventing scar stricture after papillotomy or ampullotomy. If the surgeon is impelled to open the duodenum because of some abnormality encountered in inserting the tube, additional pathologic conditions might be found

which might otherwise have been overlooked. It is hoped that the patients' hospitalization and convalescence will be smoother and considerably shortened if this technique is adopted.

Some surgeons have advised closing a common duct without drainage when normal conditions are found after exploration,[17] but most surgeons routinely insert a T-tube. Our procedure may be an acceptable compromise between these two extremes.

SUMMARY

The unsatisfactory results following biliary tract surgery have been reviewed and some of the specific conditions causing the postbiliary surgery syndrome listed. These all seem to be related to biliary hypertension, stasis, and infection. Certain objections to the routine use of the T-tube have been summarized and the possible relation of the use of this tube to the biliary surgery sequelae pointed out.

A technique of biliary drainage, using an indwelling Polyvinyl tube, has been devised and tested on 14 dogs. The tube passed spontaneously in every animal in an average of 12.8 days without the occurrence of bile leakage, bile peritonitis, or postoperative death. The advantages of this method have been discussed.

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UNUSUAL GRANULOMAS OF THE CECUM

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THE purpose of this communication is to describe 2 cases of granulomas of the cecum which were unusual, both clinically and histologically. Granulomas reported previously have been related to tuberculosis, actinomycosis, amoebiasis, syphilis, regional ileitis, ulcerative colitis, and diverticulitis. Therefore, such lesions were eliminated from the study of these 2 cases. Our cases may be classified under a definite group of granulomas secondary to sinus tracts and extending to a closed segment of bowel.

CASE REPORTS

CASE 1.—A 37-year-old white woman was admitted to Tripler Army Hospital, in January, 1955, for treatment of an abscess located within a paramedian scar. Adequate drainage was established. Culture of pus showed *Staphylococcus albus*. Diagnostic studies revealed no evidence of a sinus tract to the gastrointestinal or urinary system. She returned to military duty three weeks after admission, and it was planned to admit her again in six weeks for elective excision of the sinus tract.

In October, 1953, 51 inches of strangulated distal small bowel was resected because it was entwined about a band near the right infundibulopelvic ligament. It was necessary to perform an end-to-side ileo-ascending colostomy. The anastomosis on the ascending colon was located 2 inches above the ileocecal valve. The ileum adjacent to the ileocecal valve was closed and inverted into the cecum. A three-layer closure was made using two layers of cotton. Although the appendix was not diseased, an appendectomy was performed. The pathologic diagnosis was gangrenous necrosis of the ileum. There was fibrosis of the appendix. The patient's postoperative course was stormy, but she returned to duty two months following admission. In May, 1954, she was admitted in order to evaluate some vague neurologic symptoms. A complete neurologic and hematologic evaluation was within normal limits.

In March, 1955, she was readmitted for an elective excision of the sinus tract of the abdominal wall. The base of the tract was attached to a mass of omental tissue which measured 6 by 8 by 4 cm. Cross section of the mass revealed dense, grayish white tissue. The lymph nodes in the adjacent mesentery were enlarged. These nodes were firm and varied from 1 to 2 cm. in diameter. A frozen section diagnosis of the cecal mass was benign inflammatory lesion. No further exploration was made through the small wound because the abdominal wall sinus had contaminated the field. The pathologic diagnosis on the cecal biopsy was inflammatory granulomatous lesion with foreign body (cotton) granulomas.

During the three-week postoperative course many diagnostic studies were made because there was suspicion of a malignant lesion. Two barium enemas were normal. Sigmoidoscopy was normal. Laboratory analyses revealed no ova or parasites in the stools. The white blood count remained 8,000 to 9,000 with 70 per cent neutrophils. The eosinophils varied from 5 per cent to 14 per cent. No anemia was noted.

Laparotomy was performed in April, 1955. The large bowel had been prepared for a probable right colectomy as the diagnosis was still presumed to be carcinoma of the cecum. A long, paramedian incision was made to facilitate exploration. The peritoneum was thick and granular. Multiple dense adhesions were noted. Much to the surprise of the surgeon, the large mass expected in the cecum had diminished in size and was now only

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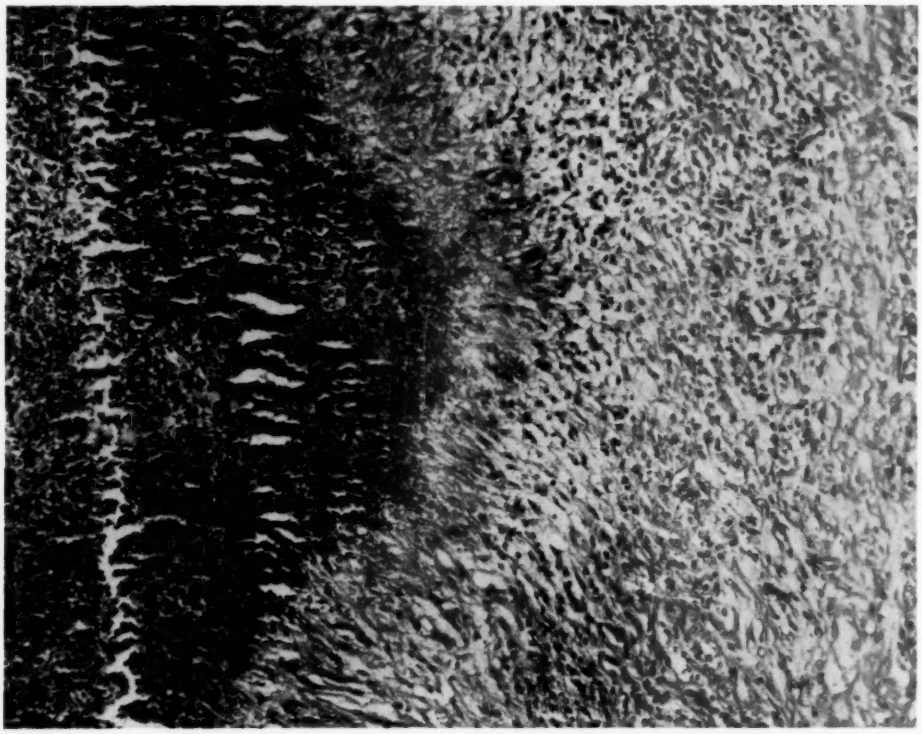

Fig. 1.—Photomicrograph of sinus within the cecum showing purulent exudate. The sinus is lined with granulomatous tissue which is densely infiltrated with polymorphonuclear leukocytes.

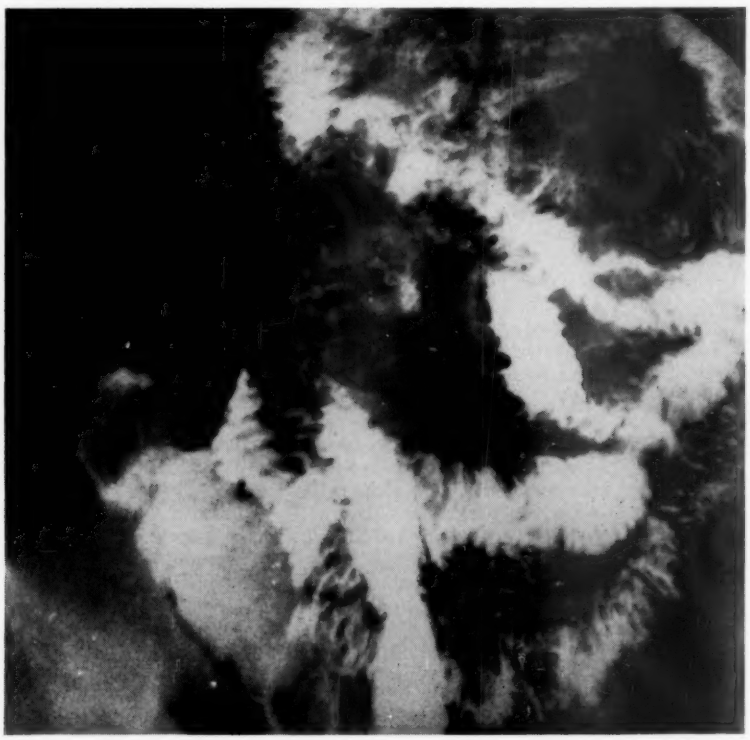

Fig. 2.—Barium study demonstrating a narrowed cecum with a proximal dilated segment of ileum consistent with obstruction.

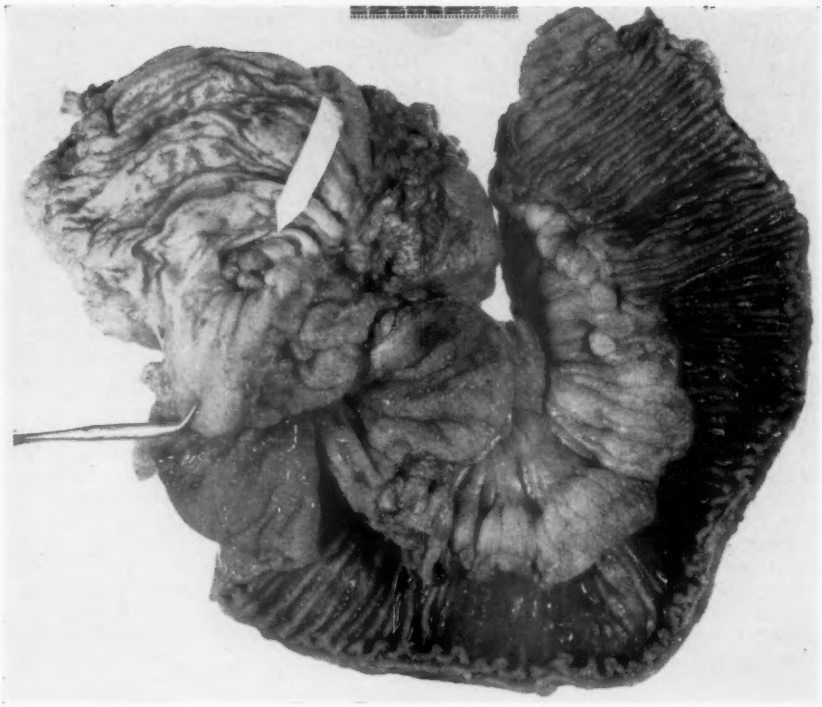

Fig. 3.—The arrow points to the mucosal surface of the sinus within the cecum of the resected tissues. The dilated proximal ileum is caused by the obstructing mass.

Fig. 4.—Photomicrograph of cecum showing the appendiceal sinus within its wall with adjacent granulomatous reaction.

3 by 2 by 2 cm. (one-sixteenth the original size). This was removed and a two-layer intestinal closure was completed. The lymph nodes in the adjacent mesentery were much smaller and softer than previously. The pathologic diagnosis of the cecal mass was sinus tract and foreign body (cotton) granuloma of the cecum. There was a sinus tract extending from the mucosa of the cecum through the muscularis and into the subserosa. This was lined by granulation tissue heavily infiltrated with leukocytes, including many eosinophils (Fig. 1). Around the sinus tract was fibrous scar tissue and foreign body granulation. The foreign bodies were cotton fibers. Inverting a segment of ileum into the cecum produced this end result.

The patient's postoperative course was very good. She was discharged four weeks after admission. When seen nine months later she had gained strength and weight and had a good appetite. She remarked: "I feel the best I have felt in two years."

CASE 2.—A 30-year-old white man was admitted to Tripler Army Hospital with a history of intermittent abdominal cramps for one month in the right lower quadrant, deep to an appendectomy scar. An appendectomy had been performed seven years previously. Barium enema was normal, but radiologic study of the small bowel showed an obstructing lesion in the ileocecal region (Fig. 2). Blood studies were normal.

Surgical exploration of the ileocecal region revealed a firm mass which measured 4 by 5 by 6 cm. The mesenteric lymph nodes were enlarged and indurated. The lesion was considered malignant. A right colectomy with end-to-end ileotransverse colostomy was performed. The postoperative course was uncomplicated. After six weeks the patient returned to duty.

The specimen revealed a sinus extending from the cecum through an old appendiceal stump, with a patent lumen to the ileum. There was a cluster of inflammatory, granulomatous, mucosal polyps in the cecum where the sinus tract entered, measuring 1.8 cm. in diameter (Figs. 3 and 4). The chronic inflammation and fibrosis had caused obstruction at the ileocecal region. There was no evidence of regional ileitis. The lymph nodes showed reactive hyperplasia.

DISCUSSION

Cecal tumefaction by abscess associated with appendicitis is well recognized. In rare cases this lesion may become embedded in dense fibrous tissue and cause symptoms. Often the first symptom noted is a tender abdominal mass (Musgrove and Dockerty[4]). The appendix is usually surrounded by or adjacent to the granuloma. There is a secondary reactive perityphlitis. The appendix is usually located in a retrocecal or retroileal position (Wilson and associates[8]). The inflammatory process is sealed off quickly. The patient does not develop progression of symptoms because the parietal peritoneum is protected from such an inflammation.

A few scattered cases of inflammatory tumors of the cecum which are unrelated to the appendix have been reported by Powers,[5] Lazarus,[2] Bargen and Jacobs.[1] Lazarus stated that an inflammatory tumor of the cecum has frequently been associated with intramural abscesses. Spivak and Busch[6] showed that primary typhlitis is a definite entity. The tumor mass is characterized by granulation tissue showing varying stages of fibroplastic changes.

Inflammatory granulomatous cecal tumors have been attributed to nonabsorbable sutures used during appendectomy. Mock's case[3] occurred three years after an appendectomy in which a linen purse-string suture was used. Tietze[7] had a similar case caused by a silk suture. Wilson and associates reported a case which resulted from linen and silk sutures. These foreign bodies were the nidus for inflammation and formed the center of an intramural abscess.

The residual appendiceal stump deserves emphasis as a cause of cecal granulomatous tumor. Wilson and associates reported 2 cases. In one case, the granuloma formed about a short remaining appendiceal segment. In the

other case, the lumen of the stump was filled with pus, the walls were fibrotic, and there was inflammation about the distal end of the stump which had apparently leaked.

Case 2 of this report is similar to Wilson's in that a granulomatous fibrous mass developed about an appendiceal stump. There was a sinus tract extending from the cecum, through the appendiceal stump to the ileum. It is postulated that the lesion resulted from the abscess which developed about the stump and then eroded into the ileum after appendectomy, which had been performed seven years previously. The patient was apparently asymptomatic until he developed intestinal obstruction secondary to the ileocecal mass.

To our knowledge, a lesion similar to that of Case 1 had not been published in the literature, that is, a cecal granuloma developing about an inverted stump of ileum. The lesion was first discovered when a sinus tract burrowed through the laparotomy scar. There was a sinus tract within the ileal stump, and the stump was the center of the granuloma. Small foreign body granulomas were also present about the cotton sutures. Within four weeks following initial surgery, the size of the granuloma had decreased considerably. Local resection of the cecal mass proved adequate.

SUMMARY

Two unusual cases of inflammatory granulomas of the cecum are presented. The common etiologic factor was a blind tract which extended into a closed inverted segment of bowel. In Case 1, a foreign body (cotton) granuloma formed at the site where the ileal stump had been inverted into the cecum seventeen months previously. Excision of the stump and granuloma was performed in two stages. The outcome of these operations was quite satisfactory. In Case 2, inflammatory granulomatous mass developed about a sinus tract from the cecum, through the appendiceal stump, to the ileum. This mass in the ileocecal region had caused intestinal obstruction. The inflammatory granuloma had formed about an inadequately excised appendiceal stump. A right colectomy was performed. There were no sequelae.

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VIRAL VERRUCAE IN THE ANORECTUM

With Consideration of the Cancer Problem

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INTRODUCTION

IN THE concepts which this study will develop, it will be helpful for the reader to think of the anorectum as a sort of physiologic and pathologic funnel or a biochemical retort. This area possesses as rich a lymphatic ring of Waldeyer as does the nasopharynx; a profuse blood supply, and an extrinsic and intrinsic innervation which interdigitates with glomus mechanisms (physiologic arteriovenous shunts) in submucosa, and Kulschitzky cells in the mucosa. These are primary units in the chemoreceptor system, and the source of the rectal carcinoid. The dentate or anal crypt line with accompanying vestigial ducts and glands may carry endocrine as well as carcinogenic propensities. Seventy-five per cent of neoplasia in the entire intestinal tract develops in this hind-gut segment. Most of the papillary or villous adenomata are found here. This surface epithelial tumor possesses certain hybrid qualities kindred to the verrucous growths of the anal area.

Verrucae, or warts, constitute a circumscribed hyperplasia or hypertrophy of the epidermis and the papillae of the dermis.[3] For growths in the anal and genital regions the term condyloma is often used, but this may lead to confusion with condyloma latum of syphilitic origin. It is, therefore, preferable to describe the nonsyphilitic type of overgrowth as verruca acuminatum, or wart. These warts have a viral origin.[8, 11]

Verrucae acuminata of the perianal region are frequently encountered and well known.

They may also arise in the anal canal and have been described as occasionally involving the rectal mucous membrane immediately above the anorectal line.[6] However, mucosal implantation appears to be difficult without an inflammatory raw bed, for mucus secretion normally washes the wart away.

Verrucae in the anal canal may be completely asymptomatic, and discovered only as an incidental finding. At other times, warts in the anal canal are sensitive, painful, bleed profusely, and interfere with function. While this demonstration merely confirms earlier findings, it has now been possible to show that warts also frequently involve the anal crypts themselves.

At the anorectal junction, the boundary between anal epithelium and rectal mucous membrane, the anal crypts of Morgagni are encountered, up to twelve

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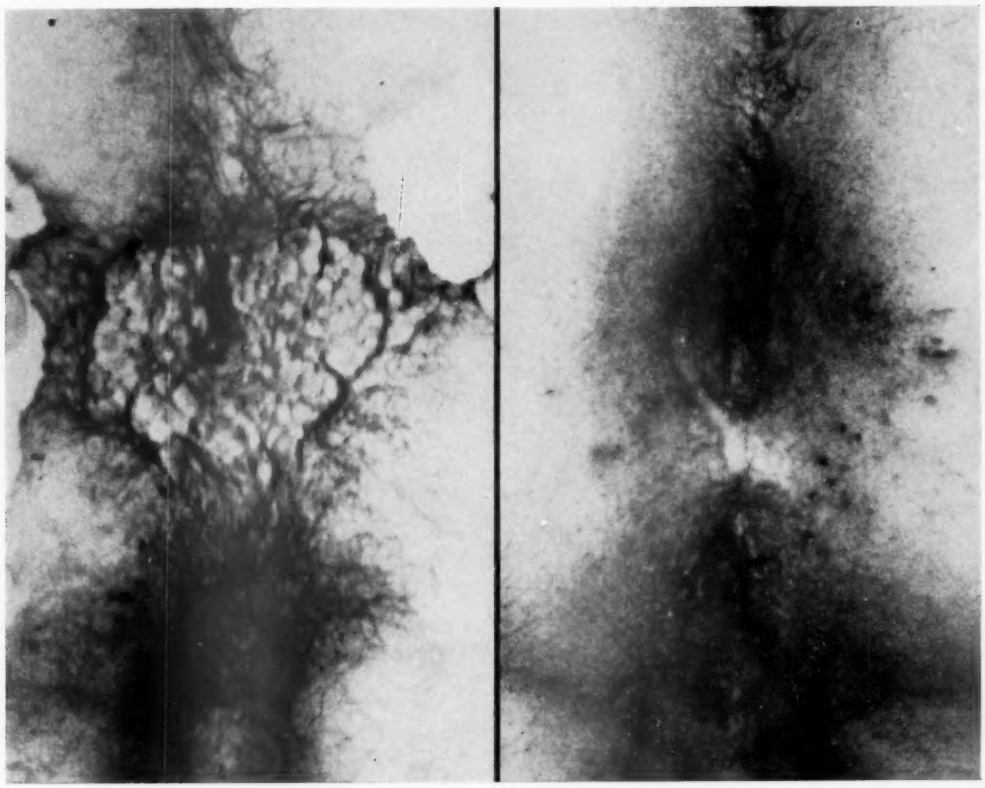
in number. They form a ring of pockets around the circumference of the anorectum with papillary elevations and intervening valves at the anorectal line. The crypts are open in the cephalad direction, and in their depths are often found vestigial ducts at the end of which small glandular structures may be situated.

The epithelium lining the anal crypts is composed of several layers of squamous cells. At the top of the valve on its deeper wall, the cells change to low cuboidal for only a cell or two and then the change to columnar mucosa of the rectal ampulla occurs abruptly.



A. *B.*

Fig. 1.—*A*, Extensive verrucae acuminata of the perianal area. *B*, Postoperative area after excision and closure and electrofulguration.

MATERIAL AND METHOD

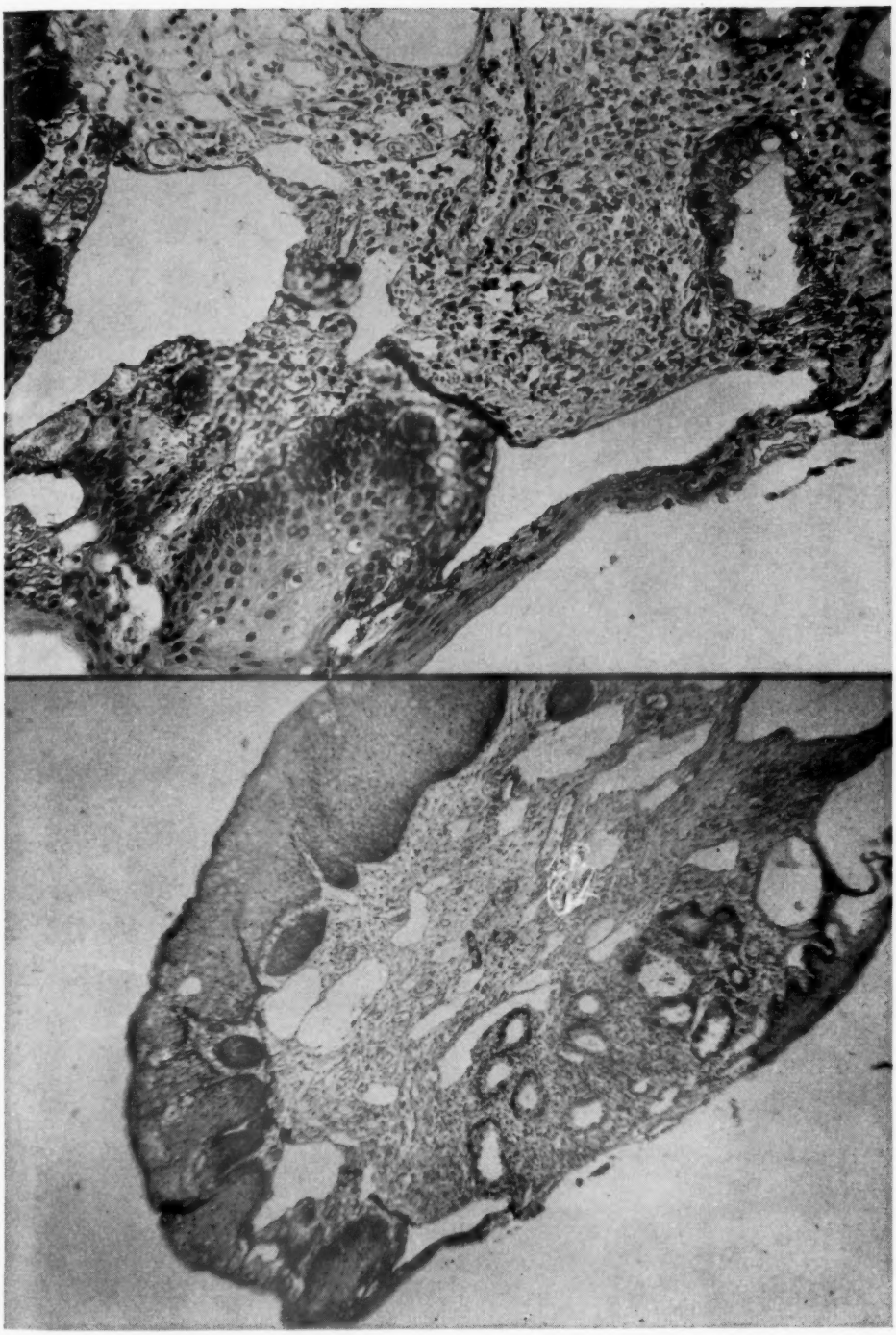
The specimens for histologic examination in this study were mostly obtained from tissues removed at anorectal surgery.* They were immediately mounted with short pins on cork boards, particular attention being paid to accurate orientation of the specimens. Where the mucous membrane of the rectum had been removed, the specimen included the involved segment of the anorectal juncture and the anal epithelium; subepithelial structures were part of the mounted material in cases of internal or external hemorrhoids, anal fissure, or fistula. The tissues were then fixed in 10 per cent formalin. On the following day, they were cut and blocked for microtome sectioning, and stained with hematoxylin and eosin.

*All microscopic material reviewed by Dr. Louis H. Winer, Department of Medicine (Dermatology), University of California at Los Angeles Medical School.

B.

A.

Fig. 2.—*A*, Wart or verruca growing in upper anal canal (×18). *B*, Higher magnification of verrucous growth in anal canal. These surface lesions are filiform, consisting of fibrous stroma covered by 5 to 10 layers of stratified squamous epithelial cells, chiefly from the granular cell layer. Many of the cells exhibit a perinuclear halo interpreted as being evidence of viral origin of such lesions. An increasing amount of basophilic staining nucleoprotein distends the nucleus itself. The stroma is edematous beneath the lesions and infiltrated with lymphocytes (×37).



A.

B.

Fig. 3.—*A*, Shows the glandular mucosa of rectum (internal hemorrhoid) with a superimposed wart on an inflammatory bed (×37). *B*, The mucosa below with the verrucous growth above showing large ballooned epithelial cells with clear spaces about their haloed nuclei (×120).

A.

B.

Fig. 4.—*A*, Anal crypt of Morgagni. Squamous epithelium lining the crypt suddenly changes to columnar epithelium (mucous membrane) at the cephalad portion of the crypt on its deeper wall. The sphincter mechanism is seen to the right of the crypt structure (×18). *B*, Vestigial anal duct and glands (intramuscular glands of Herrmann) seen dipping off from the depths of anal crypt (×26).

In the interpretation of the microscopic slides, the recent results of Blank, Buerk, and Weidman[2] were accepted as a reliable basis. This group has conclusively established the presence of inclusion bodies in warts. While these inclusion bodies cannot, at the present time, be visualized in all types of verrucae, criteria have been evolved which permit a definitive histologic diagnosis of verrucae. In the granular cell layer of the epidermis, the nuclei normally begin to disintegrate. It is in this area that the wart evidences itself. This layer, normally two to four cells thick, chokes up with ten to fifteen cells deep when invaded. The involved epithelial cell becomes ballooned and a clear space surrounds its nucleus. An increasing amount of basophilic staining nucleoprotein distends the nucleus itself. The connective tissue papillae of the dermis, containing the nourishing blood vessels, become elongated and project into the wart from below.

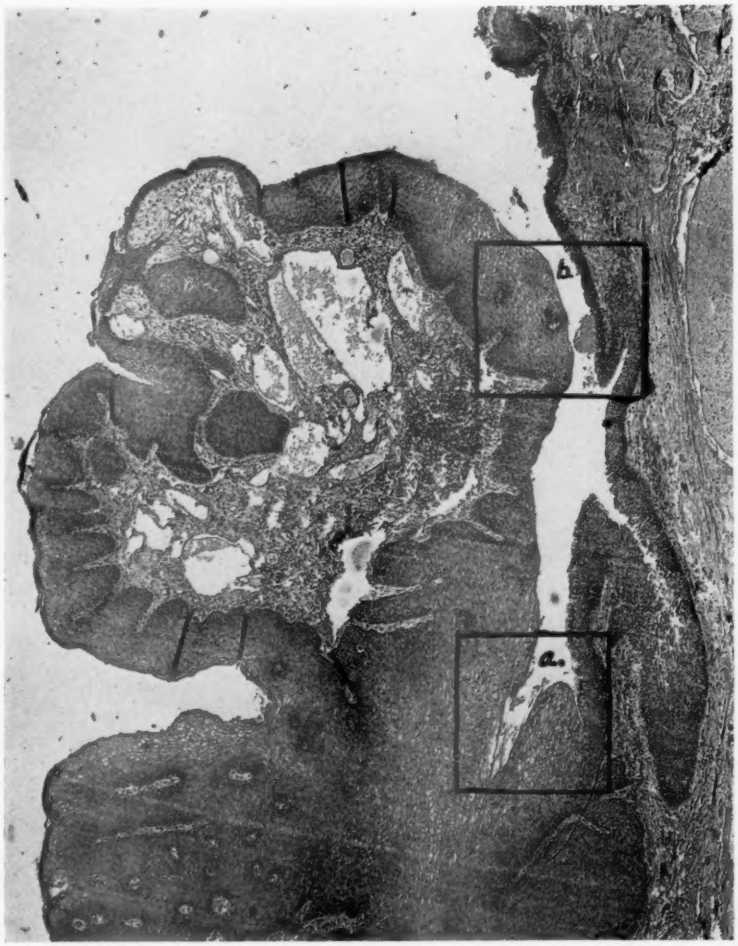
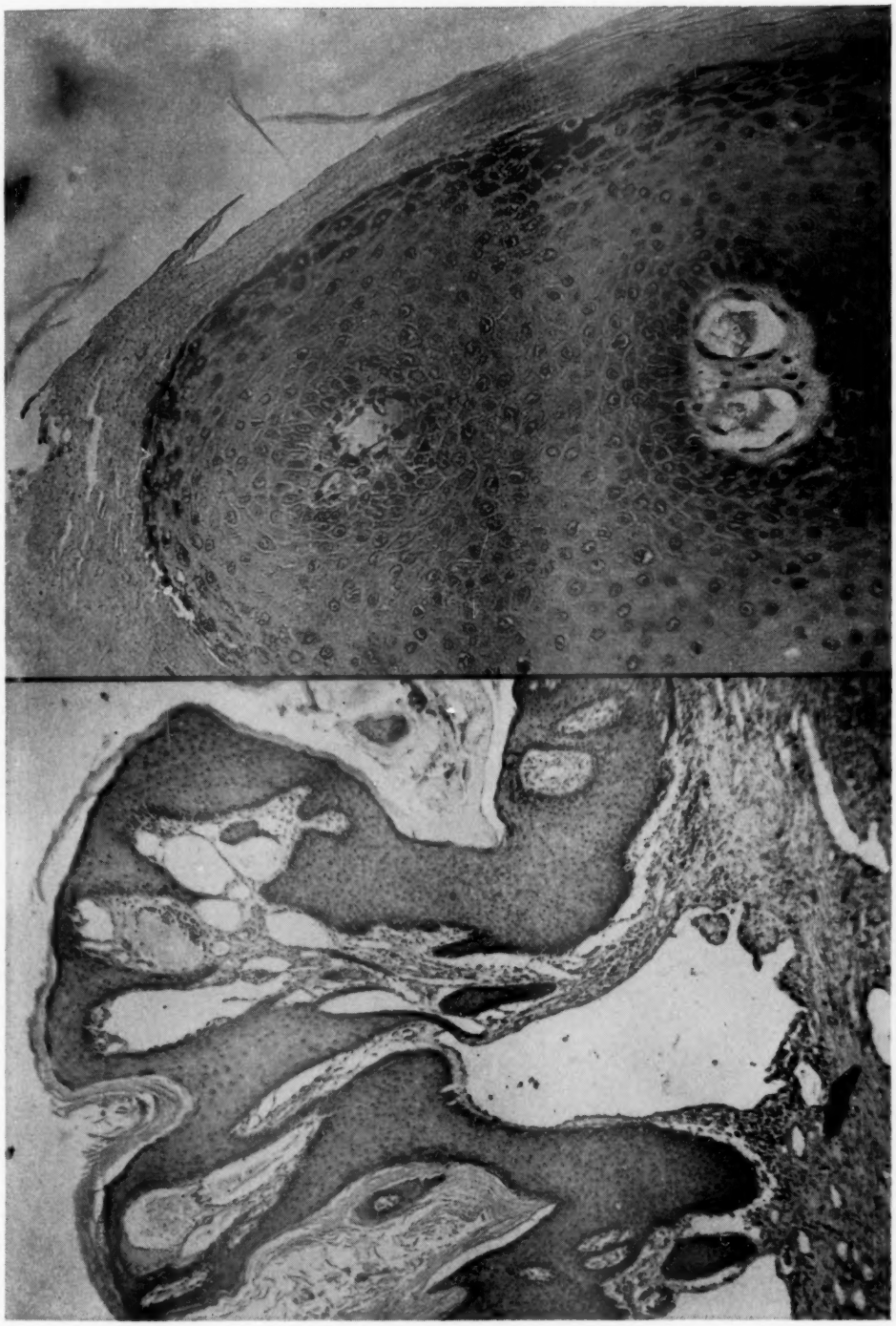


Fig. 5.—Here the outer valve of an anal crypt has been transformed into a bulbous mass (×30).

FINDINGS

In the anal crypts, verrucae have been observed plugging the lumen of this valvelike structure and interfering with adequate drainage. Thus their presence enhances secondary bacterial infection and acute anal cryptitis is initiated. The tandem sequelae of crypt disease may follow: thrombosed anal varix; anal ulcer or fissure; perianal or rectal abscess with fistula formation; and other pathologic processes due to infection.

Fig. 6.—The granular cell layer, usually 2 to 4 cells thick, is choked up with 10 to 15 layers of cells when invaded by the virus. The connective tissue papillae of the dermis containing the nourishing blood vessels become elongated and project into the wart from below. In the higher magnifications the epithelial cells invaded by the wart virus are seen ballooned with a clear space around their nuclei (×120).



A.

B.

Fig. 7.—*A*, Verrucous spicules on the tips of hypertrophied anal papillae (×37). *B*, Shows perinuclear halos in the cells deep in the substance of hypertrophied anal papillae flanking involved anal crypts (×120).

As might be expected, warts are very often found in the presence of chronic anal cryptitis. If this condition persists, the anal papillae, situated at the points of attachment of the anal crypts, may become inflamed and subsequently hypertrophied. Verrucae have been detected at the tips and in the substance of hypertrophied anal papillae.

Verrucae have also been found in anal crypts in the presence of thrombosed anal varices. Acute anal cryptitis is the forerunner of true anal fissure or ulcer which, in due time, leads to the formation of a skin-covered distal sentinel tag. Warts have been seen on the sentinel tag or in its underpocketed base.

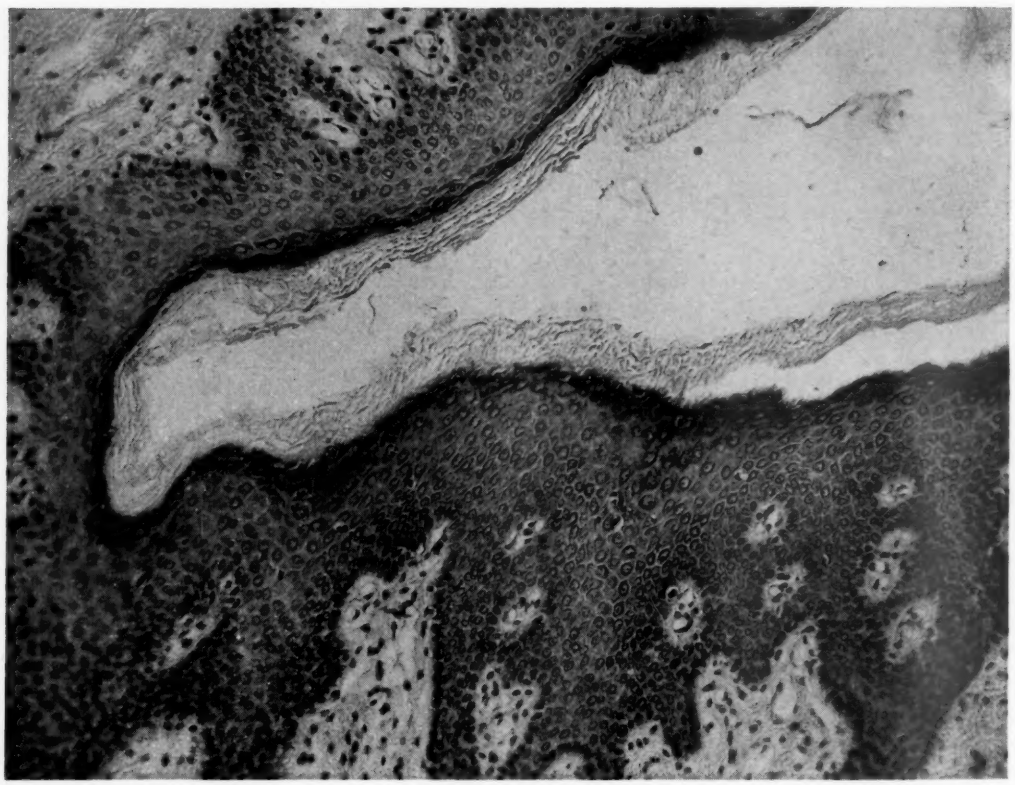


Fig. 8.—Verrucous growth in the floor or base of an anal ulcer or fissure extending into the underpocketed base of a distal sentinel tag (×120).

Another sequel of anal cryptitis is perianal or perirectal abscess with subsequent fistula.[2] Verrucae have been discovered in the core of such a fistulous tract and at its secondary orifice. Sometimes warts were seen to bulge from a deeply scarred anal crypt which was the primary orifice of a fistulous tract. The secondary opening in the perianal tissues had an operculum which, at first glance, was passed off as granulation tissue or scarring. Closer scrutiny, however, revealed the characteristic cauliflower projections of a verrucous growth which extended all along the epithelium-lined tract.

Finally, anal cryptitis enhances the development of internal hemorrhoids, and verrucae have been demonstrated growing on the surface of the mucous membrane of eroded and prolapsing internal hemorrhoids (see Fig. 3).

CLINICAL FEATURES

Warts in the anal crypts are often found in patients with a *short* anal canal. In a series of 300 patients with warts in the anal canal or crypts demonstrated clinically, more than two thirds presented this congenital variation. Obviously an anal canal of a length less than three-quarters of an inch predisposes to trauma and/or extraneous infection. It should be stressed that anal cryptitis is much more prevalent in subjects with a short-type anal canal, and the same holds true with regard to the incidence of warts in the anal crypts.

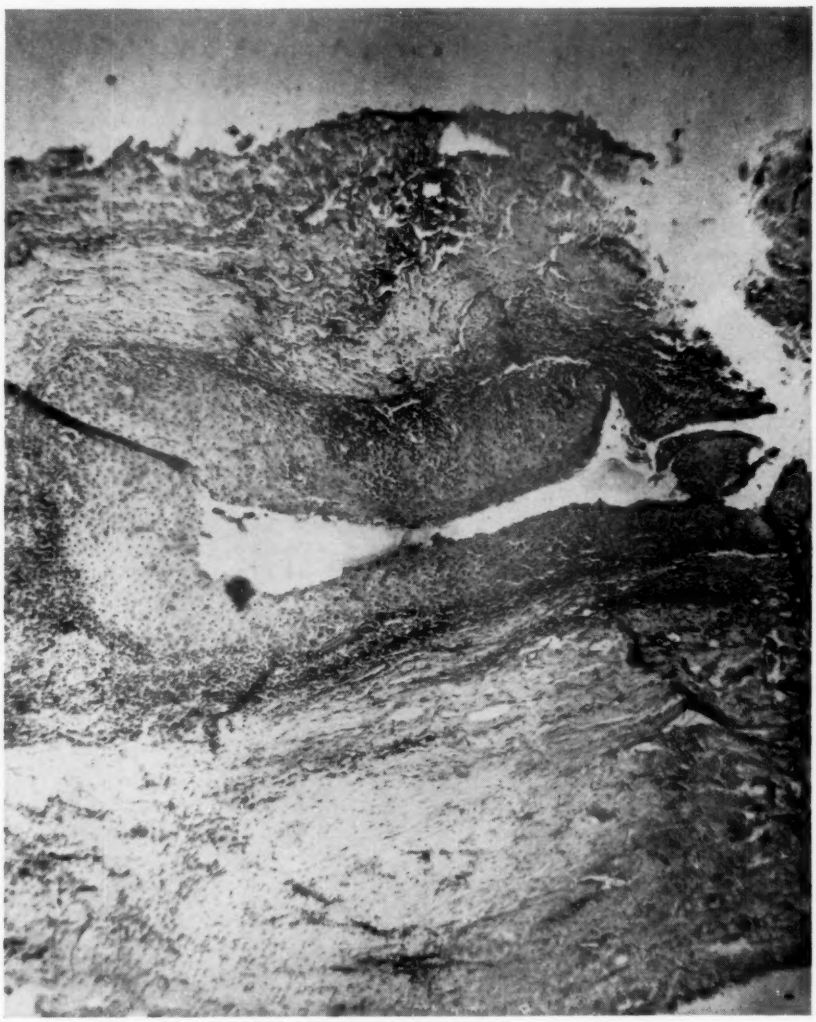


Fig. 9.—Shows in cross-section verrucous material lining a fistulous tract (×37).

Warts of the anal canal, and of the anal crypts in particular, are of great significance when anorectal surgery is contemplated. When verrucae are found upon examination and merely fulgurated at the time of surgical intervention, or when no special attention is given to seemingly insignificant warts in the anorectal region, postoperative complications are likely to develop.* In order

*Occasionally, colostomy or ileostomy stoma will become infected with verrucae, and the condition is difficult to control with the ileostomy bag in place.

to forestall increased morbidity in anorectal disease, anal verrucae should be recognized and treated before proceeding to surgical intervention. Many times when verrucae are eliminated in the presence of hemorrhoids or fissures, it will be found that the whole climate in the anorectum improves.

In addition to the numerous cases in which verrucae can be actually demonstrated, there are others in which viral involvement is merely suspected. Many patients undergoing anorectal surgery present no gross evidence of verrucae, but postoperatively the wound is reluctant to heal, even with adequate drainage of the wounds to the outside and faithful follow-up examinations. In these cases the granulating wound bed shows tiny hillocks, and appears more viscid than usual. When finally epithelium or scar tissue has covered the tract, it is of grayish hue, and often has a hatched or herringbone appearance. This tissue is not stable and frequently breaks down. Such a finding furnishes evidence of an unrecognized or untreated verrucal involvement.

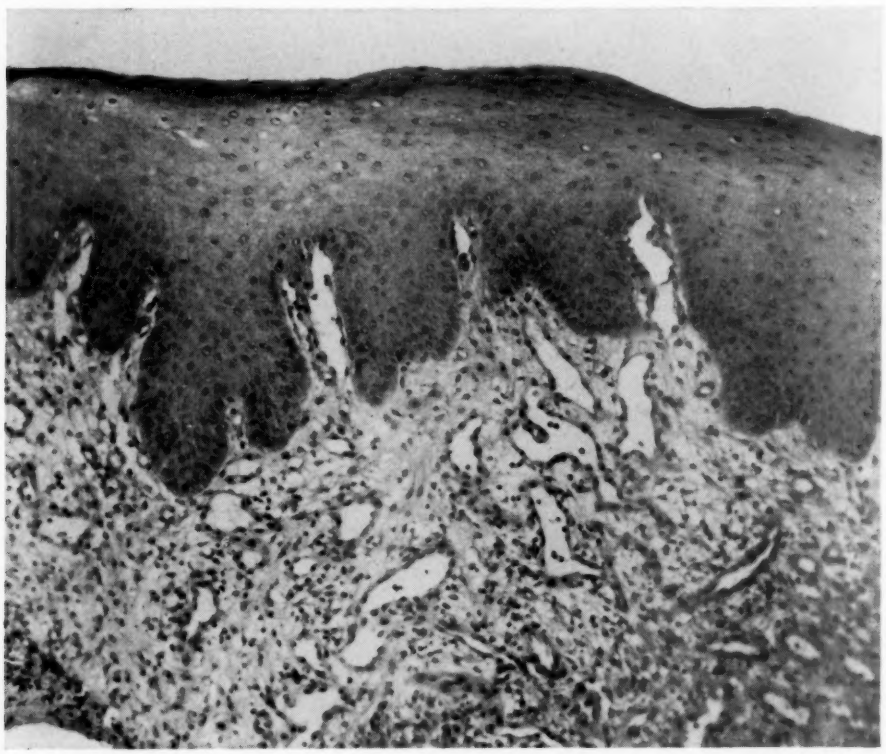


Fig. 10.—Biopsy of unstable epithelium in postoperative hemorrhoidal wound, showing ballooned epithelial cells with haloed hyperchromatic nuclei. The dermis is very vascular in the present healing process (×100).

DISCUSSION

The demonstration of verrucae in anal crypts concomitant with cryptitis poses the question of a possible added etiologic significance of warts in the development of cryptitis. The decision is difficult, as verrucae are encountered in the anal canal or in anal crypts producing few, if any, symptoms and disappearing spontaneously or with little treatment. Occasionally, one may see

during routine examination a hypertrophied anal papilla with a verrucous tip or verrucae in the crypts while the patient presents no particular complaints. The same finding in another subject may be associated with severe recurrent episodes of perianal dermatitis with pruritus and other anorectal problems.

All that can be safely said at the present time is that verrucae of the anal canal and crypts may be encountered with or without cryptitis and its sequelae Conversely, cryptitis and its sequelae may be encountered with or without evident concomitant verrucae in the anal canal and crypts. Whenever verrucae concomitant with cryptitis are present, they are likely to enhance the inflammatory process; to prevent simple resolution and to lead to one or several of the more far-reaching sequelae of cryptitis. On the other hand, dormant viral involvement of the anal tissues may be activated through acute anal cryptitis with other tandem pathologic processes.

While thus the etiologic link between anal verrucae and cryptitis still escapes precise definition, another aspect of warts in the anal canal and crypts can be discerned. Verrucae, like any other type of new or abnormal growth, draw on the available rich blood supply and invade the local lymphatics and, in this manner, tend to upset still further the physiologic balance in the anorectal area. This seems to account for the finding that any infectious process may be aggravated in the presence of anal warts.

Verrucae probably stimulate some type of immunologic reaction, especially in the anorectum. It is much too early to make any definite claims, but it is interesting to note that in a series of 300 cases of verrucae in the anal canal and crypts, not a single patient presented concomitant evidence of adenocarcinoma, squamous-cell carcinoma or villous papilloma. On the other hand, adenoma (benign polyp) of rectum or colon was observed in 28 patients. By contrast, in a series of 300 cases of carcinoma of the colon and anorectum, there was not a single instance of verrucous involvement of the anorectum. While such figures are merely suggestive, they nevertheless point the way to a problem for further study.

TREATMENT

The treatment for verrucae of the anal canal and crypts is admittedly still inadequate. Warts of large size are treated by fulguration and, occasionally, excision.[4] Lesions are carefully coated with 25 per cent resin of podophyllin in acetone or in compound tincture of benzoin, but not mineral oil. Oral administration of Bistrimate (sodium bismuth triglycollamate) has been suggested.[5, 7, 9, 10] Vaccinia has been used. Autogenous vaccines of the verrucous material should be considered.[1]

CONCLUSIONS AND SUMMARY

1. Verruca acuminatum is of viral origin in contradistinction to condyloma latum which is due to syphillis, and there is no relationship between the two conditions.

2. More than 300 cases have been carefully studied where verrucae acuminata, or warts, were found in the anal canal, anal crypts, or on rectal mucous

membrane. Most of the microscopic material studied was obtained at anorectal surgery. The specimens were mounted on cork boards to facilitate the identification of anal crypts, epithelial and mucous surfaces, and pathologic processes.

3. *Verrucae, or warts, were observed growing from the anal crypts.* The growth often plugged the crypt, thus impending drainage and enhancing secondary bacterial infection. The tandem sequelae of crypt disease, namely, thrombosed anal varix, anal fissure or ulcer, and perianal or rectal abscess with fistula formation, were noted in many instances.

4. In chronic anal cryptitis with papillitis, verrucae were detected on the tips and in the substance of hypertrophied anal papillae.

5. Verrucae were found in the beds of anal fissures and in the undermined bases of distal sentinel tags. Warts were identified in the involved crypts which served as the primary orifices or points of origin of fistulas. The verrucae were found in the substance of the cordlike tracts and were seen bulging from or plugging the secondary orifices of the fistulas.

6. *More than two thirds of the cases studied demonstrated shorter than normal anal canals.* This may be a congenital variation and predisposes to trauma, ectropion, and infection with bacterial, mycotic, and viral agents of the anorectum.

7. Recognition and adequate treatment with podophyllin in acetone but *not* mineral oil, and/or fulguration of warts and possible autogenous or vaccinia vaccine are suggested. Their elimination often promotes a more healthful climate in the anorectum with the resolution of bacterial infection and pelvic lymphatic congestion.

8. Adequate treatment by preoperative management and by fulguration of verrucae at the time of surgery often enhances postoperative recovery in all types of anorectal surgery.

Postoperatively, unrecognized or superimposed verrucous infections cause indolent scar formation. Heretofore, wounds considered to be an overgrowth of granulation tissue are now often *known* to be complicated by a viral wart formation. The unstable herringbone pattern of the scar tissue on microstudy demonstrates a verrucous pattern.

9. Verrucae in the anorectum may stimulate an antiviral or other immunologic reaction. In the 300 cases where warts were found, there was no concomitant carcinoma, although 28 instances of benign adenoma were noted. Conversely, in another series of 300 cases of carcinoma of the colon and anorectum, there were no verrucae of the anorectum found.

It is hoped that this study will stimulate a more painstaking examination and recognition of verrucae in the anal canal, and especially in the anal crypts and papillae. Finally, the relentless search for new leads in the cancer problem must be found. The presence of warts in the anorectum and the absence of carcinoma in the bowel suggests the existence of a delicate immunologic balance which must receive further concerted study. Also, should an interrelationship be definitely established, then a cancer detection test can be envisioned on this basis.

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INCARCERATED INGUINAL HERNIA WITH CHYLOUS ASCITES

A Case Report

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A REVIEW of the recent English literature fails to reveal a recounting of this situation. Incarcerated hernias are not rare, but the timing in relation to meals must be exact in order to obtain chylous ascites in a hernial sac. The return lymphatic flow from the intestines starts in small vessels called lacteals. In the fasting state these are not visualized on the gut surface. After a meal, especially one containing fat, these vessels become visible. Because of their high content of emulsified fat, they then appear white in color.

A man, aged 72 years, noted rather sudden pain in the left inguinal region, in the evening, following a large meal. He was seen within an hour after the initiation of the pain, and at this time was having excruciating pain in the left inguinal region. The patient had been in good health until recently, when he developed acute cholecystitis. The gall bladder was removed and recovery was uneventful. He had had a good appetite, no weight loss, and had been treated for mild heart failure with digitalis. Physical examination at the time of the acute pain revealed a mass in the left inguinal region. This mass was hemispherical in shape and measured about 9 cm. in diameter. It was very tender especially around the base. The mass did not descend into the scrotum. History revealed that the mass had been present intermittently for the past eight years and had not at any time descended completely into the scrotum. No attempt was made at this time to reduce the mass by taxis. The patient was sent to the hospital. A Levin tube was passed, and on the way to the operating room the patient vomited copious amounts of previously eaten food, and the Levin tube. While on the operating table the Levin tube was reinserted and attempts made to keep it functioning, but it was difficult to do because of the presence of large particles of food. Because of the patient's incipient heart failure, and a recent meal, it was decided to use segmental anesthesia. The patient was turned on the right side, and the left side was prepared in the lumbar region and over the lower ribs. The mixed nerves were injected with 2 per cent procaine as they issued from the intervertebral foramina of the first, second, and third lumbar vertebrae. Subcostal and intercostal block of the eleventh and twelfth thoracic vertebrae was then accomplished using 2 per cent procaine. The patient was placed on his back and the abdomen prepared and draped. The proposed line of inicision was infiltrated with 1 per cent procaine. After this infiltration no further anesthesia was used throughout the procedure. On opening hernial sac, a large quantity of milky-white fluid was encountered. There was approximately 18 inches of small bowel in the sac, slightly bluish in color and with whitish injected lacteals on its surface. There was no evidence of irreversible compromise of the bowel in the sac or the bowel adjacent the external ring. There was an estimated 400 to 500 c.c. of this milky fluid in the hernial sac. There was no pain at any time while manipulating the bowel. The bowel was replaced in the abdomen and the hernial sac freed out by sharp and blunt dissection. The standard operation for obliterating the inguinal canal was accomplished, and the cord transplanted to the subcutaneous tissue.

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The patient had an uneventful recovery and was not given antibiotics. The abdomen remained soft, bowel tones returned the morning of the second day, and on the third day the patient returned home. In addition to the unusual finding of a chylous ascites in a hernial sac, it is felt that the type of anesthesia used here is worthy of mention. The method of injection of the nerve is beautifully illustrated and written up in Pitkin's book on *Conduction Anesthesia.* In the past, segmental anesthesia has been used in poor-risk patients with inguinal hernia and on every occasion has been found very satisfactory to both patient and surgeon.

The sequence of events in this case is felt to be as follows: Following a large meal several loops of bowel became incarcerated in the hernial sac with the subsequent development of partial obstruction. During this time the lacteals became injected and there was an outpouring of chyle from the lacteals. The constriction at the hernial opening was not at any time enough to obstruct the bowel completely in either the proximal or the distal loop, but was sufficient to cause a lymphostasis in the intestinal wall. It should be mentioned that there was no issuance of chylous material from the abdominal cavity after reduction of the hernia. The appearance of the material was at first suggestive of purulent substance. However, because of the failure of fibrin to develop on standing, the presence of prominent lacteals, and the chalky-white appearance, it was felt that this was chyle. Furthermore, enough time had not elapsed for the development of purulent exudate, and the subsequent course of the patient rules out peritonitis.

BILATERAL MIXED TUMORS OF THE SUBMAXILLARY GLAND

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MIXED tumors constitute the largest single group in the classification of the major salivary gland tumors. However, they remain infrequently encountered lesions. Even more rare is the occurrence of more than one such tumor in an individual. It is the purpose of this paper to present the findings in a patient with bilateral mixed tumors of the submaxillary glands.

The over-all incidence of this type of tumor may be estimated from the report of the Head and Neck Service of the Memorial Hospital, New York City, as published by Frazell.[3] In an average of 2,200 patients seen on this service annually, 5 per cent were subsequently found to harbor mixed tumors of the salivary glands. Of these mixed tumors, by far the largest percentage occurred in the parotid gland (87.3 per cent). The submaxillary gland harbored mixed tumor in 12.2 per cent, and the sublingual gland in less than 1 per cent. This has been the experience of other investigators in the field: McFarland[7] in 1936 collected 300 cases, of which 93.6 per cent were parotid, 6.1 per cent submaxillary, and 0.3 per cent sublingual. Robbins,[10] in 36 cases, found 32 parotid, and 3 submaxillary mixed tumors. Marshall and Miles[6] (100 cases), Taylor and Garcelon[13] (143 cases), and Brown and his associates[1] (149 cases) have reported essentially the same distribution.

Of considerable interest is the report of Marsden[5] of 60 cases of mixed tumors from Malaya. In this geographic area, mixed tumors constituted 4.5 per cent of all neoplasms, with 30 per cent of these mixed tumors being located in the submaxillary gland. Sixty-seven per cent of these patients were Chinese, 21.5 per cent were Malays, and 11.5 per cent were Indians. Monro[8] also reported a higher incidence of submaxillary gland mixed tumors in Chinese patients. The occurrence of bilateral or multiple mixed tumors has been extremely rare. Review of the literature reveals only 6 reported instances of involvement of more than one gland in the same patient. Karl Spring,[12] in 1929, reported an unusual case of involvement of both minor and major salivary glands with mixed tumor, the patient presenting with a submaxillary lesion six years following excision of a lesion of the palate. Robbins,[10] in 1943, reported a similar case with involvement of the soft palate and parotid. Pricolo[9] in 1946, recounted a case presenting mixed tumors of both submaxillary glands, the only previously reported case of this type. Brown, McDowell, and Fryer,[1] and Wuester[14] have reported cases of involvement of both parotid glands, three distinct tumors being found in the latter's case. Slaughter[11] had a patient with a mixed tumor of the parotid who subsequently developed a lesion of the homolateral submaxillary gland.

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Discussion of the histogenesis of these tumors has been carried on through the years, and will not be entered into here. It is sufficient to say that most workers in the field now believe that the tumors arise from adult glandular epithelium with metaplasia into the various histologic pictures seen in the different parts of the tumors. Conversely, the theory of origin from rests of embryonal epithelium is felt by other investigators to be more correct. This type of discussion is difficult to resolve.

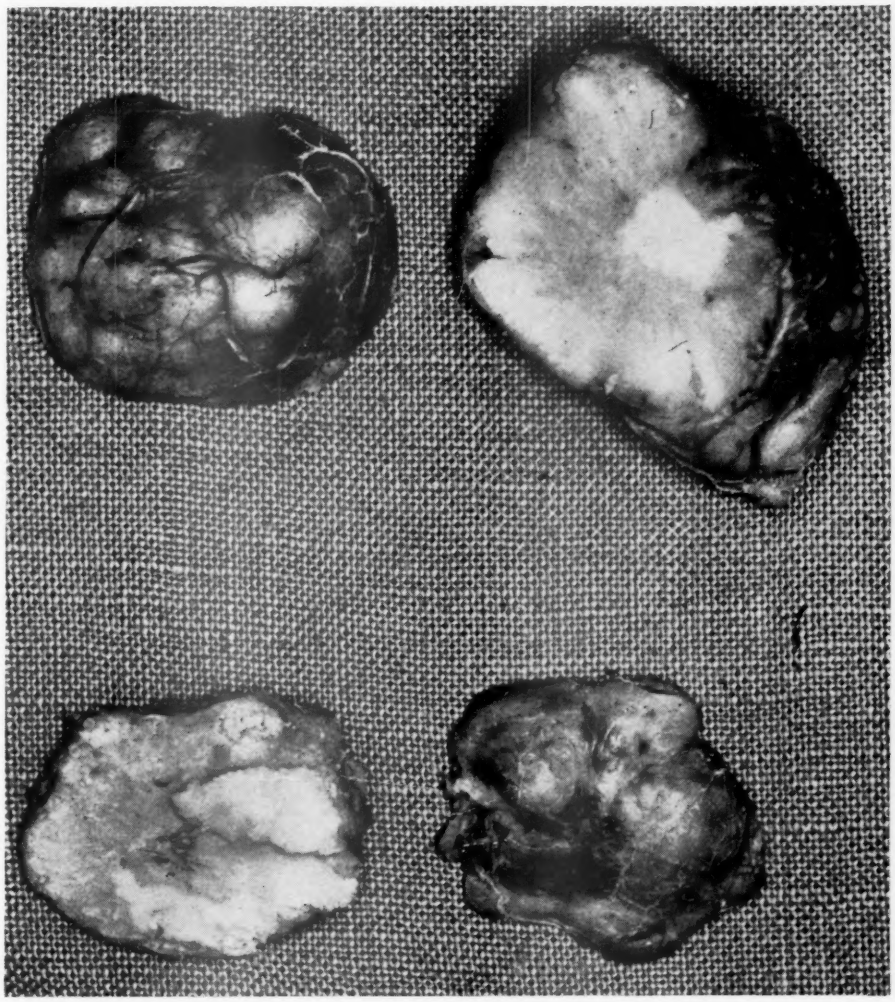

Fig. 1.—External and section surfaces of mixed tumors of right (above) and left (below) submaxillary glands. Whitish areas represent calcification.

The histologic picture of the tumors is excellently illustrated in the fascicle by Foote and Frazell.[2] The outstanding feature of the lesion is the extreme diversity of structure in different areas. In many cases, networks of spindle and stellate cells are seen, in some areas myxoid tissue predominates, and cartilaginous areas are common. Cellular portions may form tubular structures, and squamous metaplasia with epithelial pearl formation may be present. This pathologic picture was found in both of the tumors in the case presented.

CASE REPORT

CASE 1.—(Beekman-Downtown Hospital No. U-55-208) Mrs. S. B., a 38-year-old Negro woman, was first seen at the Beekman-Downtown Hospital on July 26, 1955, complaining of bilateral submandibular masses. The lesions had been noted for approximately three months, the left mass being present for one to two weeks prior to that on the right. There had been no local symptoms other than the presence of the mass. Slow enlargement of both

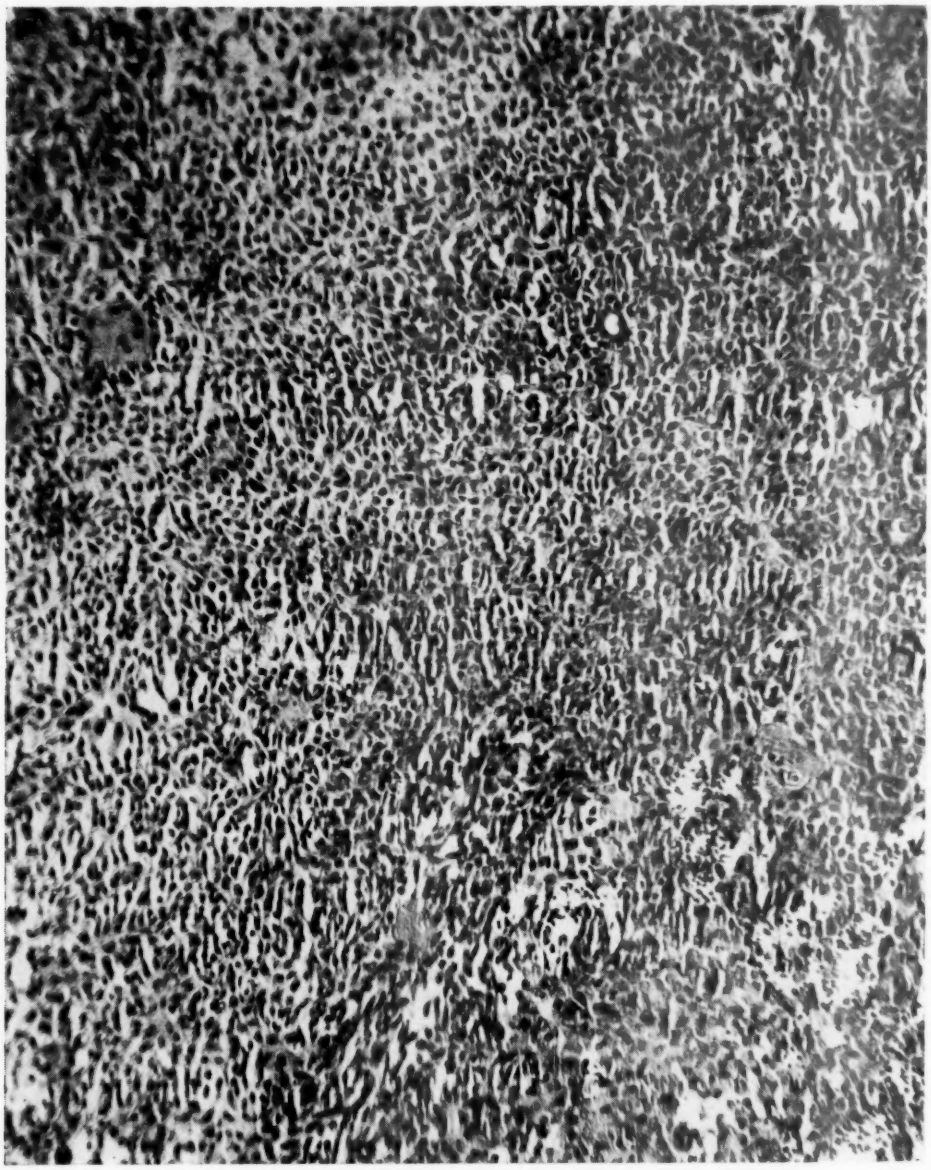

Fig. 2.—Cords and sheets of oval and polyhedral epithelial cells forming the major cellular portion of the tumors. Glandular spaces may occasionally be seen.

masses had been noted by the patient during the three months prior to admission. Physical examination was negative except for the presence of a firm, slightly irregular, nontender mass in the area of the submaxillary gland, bilaterally. There was no fixation except to the substance of the gland. The mass on the left measured approximately 2.5 cm. in greatest diameter; that on the right was slightly larger. The skin over the lesions appeared

normal. Examination of the mouth revealed no abnormalities of the tongue, gingivae, or palate. There was no cervical adenopathy. The submaxillary duct area was normal to palpation. Roentgenogram of the chest and cervical areas revealed no abnormality or calcification.

Operation was performed on July 27, 1955, under endotracheal anesthesia, with a preoperative diagnosis of bilateral mixed tumors of the submaxillary glands. Exposure of the masses, through bilateral submandibular incisions, revealed irregularly lobulated gray-yellow masses with thin capsule, involving the inferior and lateral portions of each submaxillary gland. Excision was performed through normal gland tissue, leaving the bulk of each gland in situ.

The postoperative course was without incident. The small rubber tissue drain, left in each wound, was removed on the second postoperative day, at which time the patient was allowed to go home. Following removal of sutures on the fifth day the wounds have healed well.

*Pathologic Report.**—

Gross Examination: Specimen from the right side was an irregularly round, lobulated solid mass, about 3 cm. in diameter. A thin transparent capsule was present, and small amounts of salivary gland tissue were attached to one side. The external and cut surfaces revealed a lobulated, solid, whitish tumor with areas of translucent cartilage-like material, calcified areas, and small areas of hemorrhage. The specimen from the left submaxillary gland was 3 by 2 by 1.5 cm. External and cut surfaces resembled the specimen from the right side. Here calcification was more prominent.

Microscopic Examination: Sections of masses from both sides revealed a tumor of identical structure. The tumor was made up of groups of medium-sized epithelial cells with polyhedral or oval outline forming sheets, seldom cords, and rarely lining glandlike spaces of small and medium size containing pinkish homogeneous contents. The epithelial elements were separated by large amounts of pale, finely fibrillar, ground substance in which similar epithelial cells lay singly or in small groups, resembling stroma cells. In many areas, there was cartilaginous metaplasia. Elsewhere, tissue resembling osteoid was seen; and in still other places, there was squamous metaplasia with formation of small pearls of keratin. Epithelial elements throughout oppeared well differentiated. No mitotic activity was noted. Areas of hemorrhage and hemosiderin pigment were seen here and there. Strands of collagenous fibrous tissue separated the tumor into small and large lobules. Focal calcification was seen. Decalcified preparations showed deposit of lime salts in fibrous and cartilaginous stroma but no bone formation.

Diagnosis.—Mixed tumors of submaxillary gland, bilateral and benign. July 30, 1955.

SUMMARY

A case report has been presented of the simultaneous occurrence of benign mixed tumors of both submaxillary glands in a 38-year-old Negro woman. This is the seventh report of multiglandular involvement by mixed tumors, and the second reported case of involvement of both submaxillary glands.

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HASHIMOTO'S DISEASE (STRUMA LYMPHOMATOSA)

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INTRODUCTION

IT HAS been the general impression that Hashimoto's disease is a rare entity. Following extensive investigation it has been found, however, that this disease occurs much more frequently than was previously suspected and is rather widely distributed. Its close similarity to carcinoma of the thyroid gland and its special management make it an important clinicopathologic entity to be considered in the diagnosis and treatment of the thyroid patient. It is a form of chronic thyroiditis characterized by epithelial degeneration, lymphoid infiltration, and fibrosis. This article is concerned with a series of thirty cases occurring in the Boston and Miami areas within the past five years. It is the purpose of this paper to present the various aspects relative to the diagnosis, pathologic aspects, and treatment of Hashimoto's disease.

HISTORY AND ETIOLOGY

Nonsuppurative, nonspecific thyroiditis can be classified into three categories: (1) Hashimoto's struma, (2) Riedel's struma, and (3) giant-cell thyroiditis or pseudotuberculous thyroiditis.[9]

Although Ewing,[11] in 1922, thought Riedel's struma and Hashimoto's struma represented different stages of the same disease, Graham,[13] in 1931, showed them to be clinically and pathologically distinct.

From specific forms of chronic thyroiditis (i.e., tuberculosis, syphilis, actinomycosis, etc.) the nonspecific are differentiated by the absence of evidence of specific causal organisms and by the special physical characteristics of the thyroid enlargement in these several diseases.

The replacement of thyroid tissue by lymphocytes in the thyroid gland was first described, in 1912, by Hashimoto,[15] a Japanese surgeon. Hashimoto graduated from Yale Medical School and returned to his native Japan, becoming a general practitioner in Tokyo. He treated a woman, about 45 years of age, with swollen glands in her throat, and described a condition that he had never seen before; subsequently, the disease was named after him. He later described four cases, all in elderly women. Because the lymphoid tissue was so abundant, Hashimoto himself gave this disease its most commonly used descriptive term, "struma lymphomatosa." Although Hashimoto first stressed the peculiar lymphoid infiltration of the thyroid gland in these cases, it was not until several years later that the peculiar changes in the epithelial tissue of the acini were observed. Therefore, he described only one aspect or variant of the disease.

The specific etiology of struma lymphomatosa is still uncertain, and multiple theories have been elaborated over the years. Graham[13] has been a proponent of infectious diseases and focal infections as important predisposing factors. Experimental work done on rats

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by McCarrison[27] led him to suggest that "vitamin A" deficiency was an important factor in the cause of the disease in humans, but no further evidence to support this hypothesis has been advanced.

It is of interest to note that this disease is extremely rare in men; almost 100 per cent of the cases occur in women. The reason for this almost exclusive predominance in the female is still an unanswered question. As mentioned previously, Ewing[11] in 1922 maintained that Hashimoto's disease was an early stage of Riedel's struma, and this opinion was generally favored for about ten years, when Allen Graham,[13] in 1931, convincingly proved that these two conditions were unrelated. McClintock[28] showed that the tissue of the thyroid does not change from the Hashimoto type to the Riedel type, but remains the same, as was observed by obtaining biopsy specimens from cases as long as thirteen years later. Actually, Riedel's struma is equally common among males and females.

Some authors have felt that Hashimoto's disease is a degenerative rather than an inflammatory process. The frequent functional demands in the woman during puberty, menses, pregnancies, and the menopause may, in a few cases, actually result in the gland burning itself out, with the result that lymphoid infiltration represents a compensatory replacement process for the degenerating acini. Jaffee[18] believed that any infection may lead to nonspecific degenerative changes of the thyroid gland with a secondary lymphatic reaction. It is a progressive disease, possibly associated with systemic disorders. However, excesses or deficiencies of hormone have not experimentally produced the disease.

Recently the supravital stain studies of thyroid specimens of Chesky and associates[3] have led to an entirely new concept of the etiology of Hashimoto's disease. The degenerated cells seen within the acini of the gland in Hashimoto's disease have been identified by the supravital stain as macrophages. Their studies further showed that these intrafollicular cells varied in number from one to twenty in each follicle. They were of larger size with eosinophilic cytoplasm and an oval or kidney-shaped nucleus, and they did not resemble thyroid cells at all. Animal experiments have shown that an excess of thyrotropic hormone stimulates colloidophagy in the normal thyroid. It was reasoned, therefore, that lymphadenoid goiter, in which colloidophagy with infiltration of lymphocytes is the outstanding characteristic, is related to an excess of the thyrotropic hormone. They[3] have actually been able to distinguish three stages of colloidophagy. The earliest stage shows several macrophages within the colloid of the follicle, and often a small gap between the cells of the follicle wall is observed where the macrophage enters the lumen. A later stage shows ingestion of all the colloid by the presence of more and more macrophages within the lumen. Following ingestion by the macrophages of the intrafollicular colloid, the colloid is transported to the interfollicular stroma. Here the macrophages degenerate and the liberated colloid attracts lymphocytes and gives rise to the typical lymphocytic infiltration. The chemical constitution of the colloid has become altered in such a manner that the liberated colloid now contains substances which attract lymphocytes.

The degeneration of follicle epithelium in the stages of struma lymphomatosa was interpreted by Chesky[3] as due to the pressure effect of the lymphocytes around and between the follicles cutting off their blood supply. In Hashimoto's disease there is much fibrosis and reduction of the parenchyma which starts insidiously. The changes are probably secondary to functional disturbances.

INCIDENCE

Hashimoto's disease may be seen in all age groups but is more frequent in women between the fourth and fifth decades. It is probably a metabolic or physiologic disease, usually occurring about the age of menopause. Shilling,[36] on the contrary, reports a 15-year-old white school girl as one of his youngest cases. Joll[19] mentions a girl aged 10 years. Bogart reported a Negro girl aged 14 years, and Hellwig[33] presented a case of a 16-year-old girl.

Lasser and Grayzel[23] report a case of a 6-year-old girl. Joll's oldest patient was a 74-year-old woman. There are only ten reports in the literature in which Hashimoto's disease was found in male patients.

GROSS PATHOLOGY

There is usually moderate enlargement of the thyroid gland. In the early case, the enlargement may be unilateral; but, as the disease progresses, the entire gland becomes involved, being symmetrical and firmly enlarged.

In the present series those cases with the lowest basal metabolic rates have the longest histories and most uniform lymphomatous change. This finding supports the theory that Hashimoto's disease is a form of hyperinvolution.[40]

The blood supply is probably slightly less than normal and Lahey hooks tend to cut through the tumor substance. It frequently simulates the pancreas on gross section.

In contradistinction to Riedel's struma, there is no adherence of the gland to outside structures. The gland is firm but does not present the degree of hardness so characteristic of Riedel's thyroiditis. Regional lymph nodes are not enlarged. The cut surface is finely granular and meaty appearing. The color of the cut surfaces varies but is usually a pinkish, tinted yellow. Very small multilobulations may be seen on the surface, which gives one the sensation of a fine pebbly feel when such a gland is palpated.

During dissection, there is very little bleeding. The normal architecture of the thyroid gland is absent. Grossly, it has a yellowish-gray appearance and is more or less homogeneous.

MICROSCOPIC PATHOLOGY

The pathologic features which characterize the disease are as follows: The primary alteration occurs in the epithelium. "The earliest changes characterized by nuclear hyperchromatism and pleomorphism and increased eosinophilia of the epithelial cytoplasm have generally been considered to be those of cellular exhaustion."[25] A diffuse lymphocytic infiltration associated with the presence of germinal lymph-follicles, most marked in interacinar tissues, are widespread with peculiar destruction of the thyroid parenchyma followed by fibrosis of a particular distribution. Somewhat similar changes of a focal type in thyrotoxic and other goiters are not accompanied by the clinical features of struma lymphomatosa. Clinically, struma lymphomatosa is associated with a tendency to progressive destruction of thyroid function leading to myxedema. The goiter itself affects all parts of the gland proportionally, and, while firm and resilient, it never becomes iron hard or woody in consistency. There is never any diffuse extrathyroid involvement of the cervical tissues. Pressure effects tend to be slight or moderate in degree in contrast to the grave pressure effects of Riedel's disease.

A typical example[19] is a firm goiter which appears in a middle-aged patient, usually a woman, and reaches its maximum in a few months. It involves every part of the gland, and causes only a moderate degree of dyspnea.

There are produced neither serious pressure effects, thyrotoxic symptoms, pain, tenderness, pyrexia, nor other inflammatory phenomena.

Microscopically, there are a dense, relatively acellular replacement of thyroid tissue and invasion of surrounding tissues by scar. The thyroid follicles appear disrupted, and the thyroid epithelial cells lie in small irregular groups.[25]

Hashimoto's struma presents a symmetrical, firm enlargement without adhesions, is yellowish-gray in color, and finely lobulated on section. Occasionally, an incidental adenoma is present. Examination of stained microscopic sections discloses a replacement of the acini to a variable degree by fully

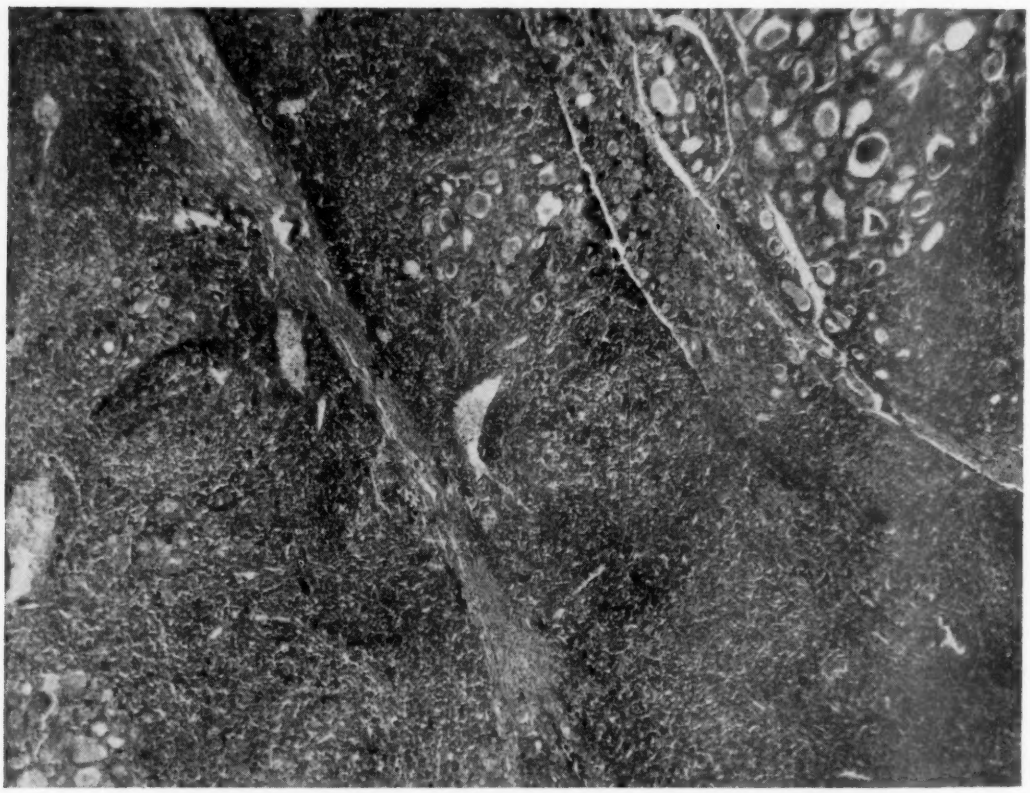

Fig. 1.—Section of thyroid tissue showing marked lymphoid hyperplasia with some germinal centers. Diminution in number of acini and those that remain show atrophy and little colloid. Slight increase in fibrous tissue also noted. (Magnification ×80, reduced ⅙.)

developed areas of lymphoid tissue with follicles. There is destruction of acinar elements. The remaining acini are small and empty, and at times show Hürthle cell formation. Sections from the same specimen show both processes, indicating that the changes in one part of the gland may be quite different from those of another. Van Hoy[40] thinks this is a coincidence and not a causal relationship. Colloid is diminished or absent.

There is a frequent formation of secondary nodules. These secondary nodules often reach a large size and ordinarily occupy the central third of a focus of lymphocytic infiltration. There tends to be a variation in the intensity

of the lymphocytic infiltration in a gland, ranging from only sparse lymphocytes scattered between colloid-containing follicles, or even absence of infiltration in certain portions of the gland, to complete obscuring or displacement of the normal architecture of confluent masses of lymphocytes, usually presenting a variable number of secondary nodules.[4] As fibrous tissue increases, the lymphoid component decreases.

Although lymphoid infiltration and fibrosis often appear to predominate in the pathologic lesion, the primary alteration occurs in the epithelium. There is reduction of the parenchyma. The earliest changes, characterized by nuclear hyperchromatism and pleomorphism and increased eosinophilia of the epithelial cytoplasm, have generally been considered to be those of cellular exhaustion.[25]

Joll[19] feels that the entire gland is involved in the process. Means[30] has reported cases of unilateral involvement which may represent a very early phase of the disease. The cells of the acini are usually small, low cuboidal, with central nucleoli. The colloid is usually present in small quantities and is entirely absent in some fields.

Moderate focal lymphocytic infiltration is present in some toxic thyroids and in some atrophic goiters of the elderly, but these are not to be misconstrued as evidence of Hashimoto's disease.

In summary, in Hashimoto's disease the cut surface has a pseudolobulated appearance. It has a firmly lobular, yellowish cast. Acini are multishaped and shrunken. The epithelium is pale and flattened. Colloid is scant to absent and vascularity is diminished. Numerous lymph follicles and plasma cells are present, with fibrosis and true germinal centers. The acini are compressed and atrophic.

CLINICAL FEATURES

This disease occurs with rare exceptions in women in the fourth and fifth decades of life. In 25,000 thyroidectomies reported by Marshall, Meissner, and Smith[26] at the Lahey Clinic, only seventy-seven cases of struma lymphomatosa were found and only one in a male. The onset is insidious. The patient complains of a painless enlargement of the thyroid gland. Such symptoms as changes in the voice, dysphagia, and irritating cough may be elicited, but these are the exception rather than the rule. When such symptoms do appear, they are most likely due to pressure from an enlarged gland. The rapidity of the progress of this disease is uncertain. It may progress slowly for many years and eventually may result in total lymphocytic replacement of all the thyroid tissue. With progress of the disease, the symptoms of hypothyroidism become manifest. In the early stage of the disease, the basal metabolism may be normal or slightly reduced, but this tends to decrease as the disease progresses. There are no significant changes in the blood count except for an occasional mild secondary anemia. The leukocyte count is usually normal. There is no fever or no regional lymphadenopathy. There may be a history of mild neck pressure.

Surgery should be conservative. The inevitable postoperative hypothyroidism varies with the individual case.

The Mayo Clinic has reported a case of lymphocytic thyroiditis which caused obstruction of the superior vena cava, resulting in a superior vena caval syndrome.[37]

DIFFERENTIAL DIAGNOSIS

The differential diagnosis with regard to cancer is important. The possibility of malignancy has either been considered preoperatively or is thought of as a possibility when the gland is exposed during operation. In the majority of cases, the surgical error is to consider such a gland as malignant and to treat it as a malignancy. The commonest surgical procedure because of this error is the total ablation of the gland, resulting in occasional untoward sequelae. It is a good rule never to perform a total thyroidectomy in dubious situations unless one has obtained a positive pathologic diagnosis for malignancy. As one attains the experience, these two conditions can readily be differentiated during gross operative examination. The malignant gland is coarsely nodular, with an irregular surface, and frequently associated with extension of the disease in the surrounding tissues. The regional lymph nodes may be enlarged due to their involvement by invasion. On the other hand, the surface of the gland in struma lymphomatosa is very finely nodular, with no extension to the adjacent tissue and no involvement of the lymph nodes. Frozen section must always be carried out to avoid error.

One can usually differentiate Hashimoto's disease from Riedel's struma because the disease tends to remain localized to the gland itself in Hashimoto's disease, whereas in Riedel's struma there is a definite tendency of the pathologic process to extend beyond the thyroid capsule. In Riedel's disease the separation of the gland from the trachea and the surrounding tissues may be a most difficult task. Whereas Hashimoto's disease tends to be confined almost 100 per cent to women between 45 and 60 years of age, Riedel's struma may occur equally in both sexes and in a comparatively younger age group. The pressure effects seen in Hashimoto's disease are usually absent or extremely mild, whereas in Riedel's struma the effects due to the "viselike grasp" of the gland about the trachea and esophagus are quite marked and may be quite serious in nature. Treatment of Riedel's struma must be surgery.

Hashimoto's disease is differentiated from the chronic thyroiditis of the giant cell type described by De Quervain and Giordanengo[10] by the absence of inflammatory reaction within the gland, by its bilateral involvement, by the tendency of the patient to exhibit hypothyroidism, and the absence of any tendency toward spontaneous cures. It is also differentiated from the specific forms of chronic thyroiditis, such as tuberculosis, syphilis, and actinomycosis, by the absence of the specific causal organisms.

TREATMENT

The consensus of most surgeons is that only enough of the thyroid gland should be removed to relieve pressure symptoms or to establish a diagnosis, thus

ruling out cancer. Too much gland should not be removed because of the possibility of producing a severe degree of myxedema.

Lee[24] has felt that Hashimoto's disease presents a perfect complex for treatment of the gland with x-ray or radium and has advocated this type of treatment with apparent good results. The question that naturally arises is whether this disease should be treated by surgery or radiotherapy. In 1932 a successful case treated by a radium collar was reported in England.[24] McSwain and Moore[29] in 1943 urged that Hashimoto's disease be treated by x-ray therapy in preference to surgery. Their argument was that surgery is unnecessary and that the degree of hypothyroidism developing from surgery is greater than that developing from x-ray therapy.

Crile[7] believes that the diagnosis can be simplified by the use of the Silverman needle. Following this easily obtained diagnosis, he advocates treatment by radiotherapy. We feel that the Silverman needle biopsy puncture should be used more often in thyroid glands of unusual nature regardless of whether one supports definitive treatment by surgery or x-ray. If one is certain of a diagnosis of Hashimoto's disease before surgery, then certainly the operator will tend to be more conservative in the quantity of gland removed.

X-ray therapy consists of two opposed lateral fields embracing the thyroid gland and the thoracic inlet. Two thousand roentgen units are applied to each field over a period of four weeks.

The best results in the treatment of Hashimoto's disease are obtained by the most conservative therapy. Radiotherapy, following biopsy, has given excellent results. The response is rapid and the gland will decrease markedly in size in two to three weeks following therapy. If surgical treatment is followed, the less tissue removed the better, provided that enough tissue is excised to relieve any mechanical or pressure effects. The results of surgery in general are good. Clamps in the gland readily cut through the lymphoid tissue. All of our patients presented in this paper have been treated by surgery. None of these cases have required secondary operative procedures on the gland for further relief of symptoms. It is true, however, that in almost every instance the postoperative patient will require several grains of thyroid medication daily in order to maintain a normal basal metabolic rate. It is important when operating on these glands to excise the pretracheal thyroid tissue widely so as to expose thoroughly the trachea, and only in this manner can one be satisfied that all the pressure has been relieved from the trachea.

Furr and Crile[12] have recently used cortisone in the treatment of several cases of Hashimoto's disease and have noted a decrease in the size of the gland within one to two months. They believe that the action of cortisone is similar to that of x-ray therapy, producing its therapeutic action by means of lymphocytolysis. These authors used thyroid extract (2 to 3 grains daily) as the only treatment for twelve cases in their reported series and have observed that in most of these cases the size of the gland shrinks almost to half the size in from four to six months. They speculate that the desiccated thyroid depresses the pituitary thyroid-stimulating hormone (TSH) which is a strong factor in producing the lymphocytic infiltration in Hashimoto's disease.

Riedel's struma fails to respond to radiation. Hashimoto's disease may respond to radiation. On the other hand, De Quervain's disease always responds to radiation.

Crile[6] advises the use of x-ray rather than surgery for treatment of Hashimoto's disease.

PROGNOSIS

Hashimoto's disease is a relatively benign disease that may give rise to mild pressure symptoms about the trachea necessitating excision of a portion of the gland for diagnosis and also enough gland to relieve pressure symptoms. Hashimoto's disease may proceed posteriorly and encircle the trachea. Whether the patient is treated or not, eventually a mild to severe degree of hypothyroidism may result which can be adequately controlled by thyroid medication. The only instance where prognosis must be guarded is where the surgical error of removing too much gland is made, resulting in an incapacitating degree of myxedema.

The number of correct preoperative diagnoses ranges from 20 to 30 per cent.

ANALYSIS OF CASES

Analysis of our thirty cases revealed that all patients were female. Their average age was 44 years. Duration of symptoms preoperatively was slightly over two years. The youngest patient was 23 years old. The oldest patient was 69 years old. Twenty-two of these patients complained of an enlargement of the neck in the region of the thyroid gland. The preoperative diagnosis in almost every instance was nontoxic adenomatous goiter, although several were thought to have solitary adenomas of the thyroid gland. In two patients, "sore throats" and "difficulty in swallowing" were the chief complaints. Preoperative symptoms consisted of dyspnea, dysphagia, or a feeling of tightness about the neck. Routine laboratory examinations revealed no abnormalities. All of these patients were subjected to surgery. The surgical procedure in every instance was subtotal thyroidectomy, conservative excision being carried out in most cases. There were no untoward sequelae and all of these patients had an uneventful convalescence and were getting along free of complaints when last contacted. Most of these patients required 1 to 2 grains of desiccated thyroid daily in order to maintain a satisfactory basal metabolic rate.

Postoperative hypothyroidism or myxedema in patients with this disease ranges from 25 to 50 per cent, and in this group it was 60 per cent.

Fifteen patients were postmenopausal.

CASE REPORTS

The following case reports are typical of patients with Hashimoto's disease:

CASE 1.—Mrs. E. M., 26 years of age, was admitted to the hospital in March, 1952, because of a mass in the neck of three months' duration. The patient stated that the mass did not cause her any discomfort and was diagnosed as a goiter by her local physician. The basal metabolic rate on admission was +6. At no time did she have difficulty in breathing or swallowing.

The physical examination showed a Grade II enlargement of both lateral lobes of the thyroid which moved with deglutition. The gland was firm in consistency, with no associated nodules in either lobe. No bruits were heard over the gland. The impression preoperatively was adenomatous goiter.

On March 6, 1952, a bilateral subtotal thyroidectomy was carried out and at that time the surgeon could not be sure whether or not the condition was malignancy of the thyroid or Hashimoto's disease. The pathologic diagnosis at that time was subinvolution of hyperplastic thyroid with marked lymphoid reaction, i.e., Hashimoto's disease. Small numbers of interacinar Hürthle cells were present in some fields. The patient's postoperative course was uneventful, and she was discharged on March 11, 1952.

CASE 2.—Mrs. G. S., a 27-year-old woman, was admitted to the hospital in July, 1951, because of a mass in the thyroid gland. There were no systemic symptoms suggestive of hyperthyroidism. Examination showed what appeared to be a solitary adenoma of the isthmus of the thyroid, nearly two inches in diameter. The diagnosis was nontoxic adenoma of the thyroid. Excision was advised because of the danger of malignancy. A subtotal thyroidectomy was performed. The patient tolerated the procedure well and had an uneventful postoperative convalescence.

The pathologic sections showed thyroid gland tissue with outstanding infiltration by lymphadenoid tissue. Lymph follicular structures containing germinative centers were present. The parenchyma showed very little colloidal content. The final diagnosis was struma lymphomatosa.

COMMENT AND CONCLUSIONS

1. The differential diagnosis between Hashimoto's struma and cancer is so "tenuous" that surgery is pertinent.
2. Hashimoto's disease must be differentiated from cancer and lymphosarcoma.
3. Frozen pathologic section is imperative at the time of surgery.
4. The usual postoperative hypothyroid state is only temporary.
5. A series of thirty patients was studied and all were found to be female. They averaged 44 years of age.
6. Hashimoto's disease predominates in women from 45 to 60 years of age.
7. Hashimoto's disease tends to produce myxedema.
8. Hashimoto's struma is extremely radiosensitive.

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UNCOVERED SCALP HAIR AS A SOURCE OF CONTAMINATION

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THE improper use of the surgical cap is noted quite commonly in hospitals in various parts of the country and also in illustrations in medical journals. Occipital and temporal hair remains uncovered when the cap has its lower border turned up or if it is poorly designed (Fig. 1). Loose hair, dust, and dandruff can readily fall into the operative field, especially when the surgeon leans over the table. Contamination from this source can be the cause of wound infections not otherwise explained. Scalp hair found in the operative field cannot rightly be assumed to have come from the autoclaved pack.

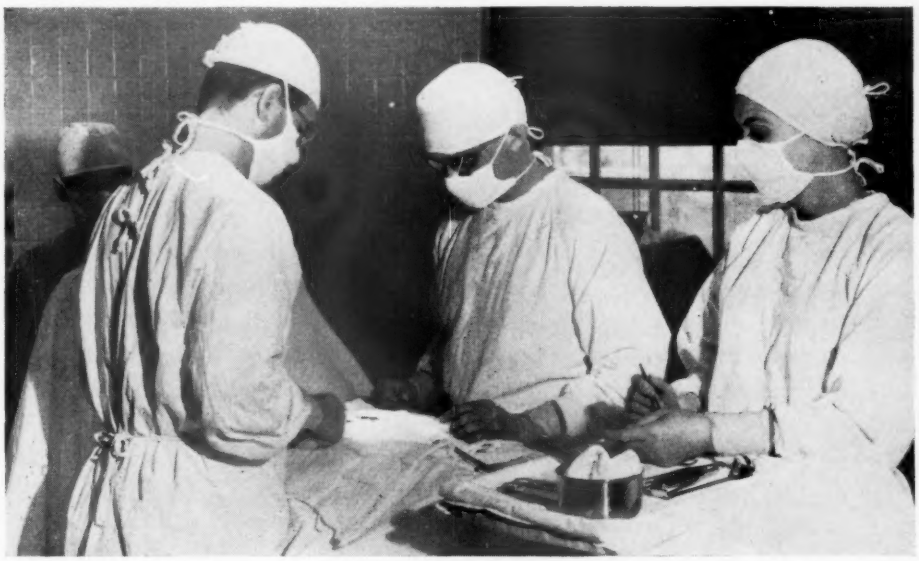

Fig. 1.—In left foreground the surgeon's cap has edge turned up and fails to cover occipital and temporal hair.

In this breach of technique, surgeons, including the resident staff, are most commonly at fault. In marked contrast to the careless attitude of these surgeons is that of the nurses whose hair is generally adequately covered, often with a hood. On the other hand, anesthesiologists not infrequently are offenders, apparently so preoccupied with their particular problems that they are not mindful of the technical requirements applicable to all operating room personnel. In this particular, most nurse anesthetists conform to surgical technique. However, in this group, there are exceptions to whom apparently the main purpose of the cap is to serve as an insignia of their position or even of their particular school.

Unexplained wound infections still occur, though decreased in incidence and severity by various technical improvements and antibiotic therapy. Precautions to prevent contamination from scalp hair should be observed as are other basic requirements of aseptic technique.

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ELECTRON STERILIZATION OF CATGUT

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THE customary method of sterilization of collagen sutures, namely, heating in a high-boiling hydrocarbon mixture named cumol, has three shortcomings: (1) Sterilization is accomplished in an open tube which, after addition of tubing fluid, usually isopropylalcohol, is sealed thereafter, so that there is a potential danger of recontamination. (2) The safety margin, or the difference between the temperature used for sterilization and that necessary to kill the most resistant pathogenic microorganisms, is very narrow. (3) The tensile strength of sutures is markedly reduced by heat sterilization; for instance, plain catgut, gauge 2-0, 3-0, and 4-0, loses an average of 12.3 per cent of its original strength, and chromic catgut of the same sizes loses 13.8 per cent.

In a search for an improved method of sterilization of collagen suture materials the use of electron irradiation suggested itself because the employment of high energy electron beams has been proved efficacious in industrial processing of foodstuffs and sterilization of pharmaceuticals and sanitary products.

In principle, all kinds of active rays can be used for sterilization purposes. Such energy can be obtained from numerous radioactive sources, such as nuclear reactors, mixtures of waste fission products, or isolated fission wastes, such as cesium or strontium. However, artificially produced electrons offer several advantages over neutrons obtained from nuclear reactors or radioactive elements: (1) absence of residual radiation or formation of radioactive by-products in the irradiated material, (2) excellent utilization of available energy, (3) type of absorption which provides a high degree of uniformity of the radiation dose, and (4) relatively low cost of irradiation.

Electrons accelerated by potentials of several million volts are capable of penetrating substances to a considerable depth. The fundamental action of high-energy electrons in destroying microorganisms begins with disturbing the natural electrostatic balance of atoms and molecules. The ionizing process leads to alterations of their chemical relationship which ultimately result in the demise of the living organism whereas the effect on nonliving collagen material remains negligible.

The present study was undertaken for the purpose of evaluation of catgut irradiated with a Van de Graaff two million-volt electron accelerator.

Scott Incline Plane tester was used for comparison of the knot tensile strength of electron irradiated chromic catgut with corresponding gauges of cumolized catgut. The results, recorded in Table I, show that irradiated catgut was from 14.6 to 26.2 per cent stronger than identical sizes of cumolized catgut.

Results of bacteriologic studies[1, 5, 6, 12] established the following descending order of sensitivity to irradiation: gram-negative bacteria, gram-positive bacteria, molds, yeast, and bacterial spores. A partial list in Table II shows that

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TABLE I. KNOT TENSILE STRENGTH OF CUMOLIZED AND OF IRRADIATED CATGUT

GAUGE	TYPE	TENSILE STRENGTH (KG.)	DIFFERENCE IN TENSILE STRENGTH (PER CENT)
1	Irradiated	5.32	
	Cumolized	4.29	23.6
0	Irradiated	3.95	
	Cumolized	3.14	26.2
00	Irradiated	2.73	
	Cumolized	2.36	14.6

some cultures of *Streptococcus pyogenes hemolyticus* remained positive after exposure to 200,000 Reps* but a dose of 300,000 Reps was bactericidal for all cultures. A dose five times greater, namely, 1,500,000 Reps, was required to exert bactericidal effect on spores of *Clostridium sporogenes.* The most resistant spores, such as *Clostridium tetani,* were killed at 2,100,000 Reps, voltage 2.5 MeV.† Inasmuch as the radiation dose employed for sterilization of catgut was 3,000,000 Reps, the safety margin was approximately 50 per cent. An additional safeguard was provided by supplementing each lot of suture material to be sterilized by irradiation, with a batch of intentionally contaminated samples, subsequently cultured.

TABLE II. RELATIVE RESISTANCE OF BACTERIA, SPORES, YEAST, AND MOLDS TO CATHODE RAYS

ORGANISM	HIGHEST DOSE SHOWING POSITIVE CULTURE (REPS*)	LOWEST DOSE SHOWING ALL NEGATIVE CULTURE (REPS*)
Diplococcus pneumoniae, Type 3	400,000	500,000
Sarcina lutea	300,000	400,000
Streptococcus pyogenes	200,000	300,000
Micrococcus pyogenes var. *aureus*	125,000	150,000
Mycobacterium tuberculosis var. *hominis*	100,000	200,000
Micrococcus pyogenes var. *aureus* (hemol.)	100,000	150,000
Micrococcus pyogenes var. *albus*	25,000	50,000
Escherichia coli	100,000	150,000
Torula histolytica	900,000	1,000,000
Aspergillus niger	300,000	320,000
Clostridium tetani	2,000,000	2,100,000
Clostridium sporogenes	1,400,000	1,500,000
Bacillus subtilis	1,100,000	1,200,000

*Reps = roentgen-equivalent-physical units.

To study tissue reaction to irradiated suture material, both plain and chromic irradiated catgut, gauges 0 and 00, were implanted in the abdominal wall and dorsal region of 15 rabbits on one side, and cumolized catgut of identical size on the other side. The animals were sacrificed three, seven, or fourteen days after insertion of sutures, and biopsies were taken for histologic studies.‡

Study of the biopsies taken on the third, seventh, and fourteenth day after implantation of suture material gave the following results. The reaction around the suture material was rather mild. Up to the seventh day, cellular response

*The term is an abbreviation for "roentgen-equivalent-physical unit," indicating that Rep is a unit of dosage which produces the same effect as 1 roentgen of x-radiation

†MeV is the energy carried by an accelerated unimpeded electron across a voltage difference of 1 million volts.

‡The histologic examination was done by Dr. R. J. Zientek, Department of Pathology, University of Illinois College of Medicine.

was primarily in form of accumulation of polymorphonuclear cells with an appreciable number of eosinophils, whereas in the 14-day-old specimens lymphocytes predominated. Variable zones of muscle necrosis surrounding the inflammatory area were probably caused not by the suture material but either by trauma produced by the needle or by compression caused by a tight suture. Surrounding the necrotic tissue there was a zone of fibroplasia. The fibroblastic activity was most pronounced on the seventh day but it continued progressing at a lower pace through the fourteenth day. There was hardly any evidence of absorption of catgut. On the whole, no substantial differences could be detected between tissue reactions to irradiated and cumolized catgut.

To test in vivo the reliability of electron-irradiated sutures, an experiment based on the following consideration was devised. Sutures in the abdominal wall are exposed to a greater stress than those placed in any other region of the body. There is no paucity of data pertaining to measurements of intra-abdominal pressure. According to numerous investigators[2-4, 7-11, 13, 14] the peak of intra-abdominal pressure raised by such factors as cough, sneezing, hiccough, gagging, emesis, meteorism, ascites, labor, strain on defecation, or any other voluntary muscular effort, lies at about 150 mm. Hg; on rare occasions it may reach 200 mm., but practically never exceeds 250 mm. Pressure developed by expiration against a closed space does not climb above 200 mm. It follows that dependable suture material must be able to stand a pressure of 200 mm. Hg.

Under aseptic conditions a paramedian incision was made through the entire thickness of the abdominal wall of anesthesized rabbits. Interrupted catgut sutures were placed 0.5 cm. apart through the entire abdominal wall, excluding the skin, which was closed separately with interrupted dermal sutures. In another group of rabbits a continuous suture of catgut was employed. In the total group of 35 rabbits the following collagen materials were implanted: plain and chromic catgut, gauge 0 and 00, both irradiated and cumolized types. The animals were sacrificed three, seven, or fourteen days after the sutures were placed. The entire abdominal wall was immediately excised and placed over a sturdy round hardwood box, 8.5 cm. in diameter. Umbilical tape was placed in a groove made in the wall of the box, around the overlapping edges of the abdominal wall so that a taut diaphragm was formed. The box had two openings with adapters, one connected with a compressed air outlet, and another attached to a sphygmomanometer. The interior of the box was rapidly inflated until the pressure reached 200 mm. and then it was quickly deflated. This maneuver was repeated 100 times and on numerous occasions the interior of the box was inflated to 250 mm. of mercury. To facilitate the observation of the effect of the distention on the catgut suture line, the skin sutures were removed in some cases. The experiment showed that both irradiated and cumolized types of catgut, plain as well as chromic, sizes 0 and 00, held when exposed to such high pressures.

The results of the animal experimentation warranted a clinical trial of irradiated collagen sutures. Plain and chromic catgut, gauges 0 and 00, were used in 76 operations, such as cholecystectomy, appendectomy, gynecologic procedures, and herniorrhaphies. In regard to handling properties, no differences could be detected between irradiated and cumolized catgut. Local or

systemic allergic reactions, dehiscence of the wound, or signs of infection attributable to the suture material did not occur.

DISCUSSION

Determination of the tensile strength of electron-irradiated catgut showed that it exceeds that of the cumolized type by from 14.6 to 26.2 per cent.

Experiments in vivo demonstrated the fact that plain or chromic irradiated catgut, in sizes as small as 00, is able to withstand repeated impacts of intra-abdominal pressure corresponding to that observed in man under various physiologic or pathologic conditions.

Bacteriologic studies proved that electron irradiation exerts bactericidal effect on all tested pathogenic microorganisms, including bacterial spores. The irradiation doses applied to the material tested exceeded the lethal dose for the most resistant microorganisms by 50 per cent, whereas the safety margin in the customary heat sterilization is only 5 per cent because the lethal temperature for the most resistant bacteria is 148.8° C. (300° F.) and cumolization is accomplished at 156.6° C. (314° F.). Another important advantage of irradiated catgut lies in the fact that the tubes containing suture material are sealed before sterilization so that subsequent contamination before their use is completely eliminated.

SUMMARY

1. Electron-irradiated catgut possesses greater tensile strength than heat-sterilized catgut.

2. The safety margin of irradiated catgut is ten times that of heat-sterilized catgut.

3. Sterilization by irradiation is accomplished in sealed containers, thus eliminating the danger of recontamination.

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Editorials

CONDUCTED BY I. S. RAVDIN, M.D.

The Strategy of Medical Research*

Medical research in the United States—its achievements and prospects—is reviewed in two fascinating volumes from the American Foundation. The second, in discussing the investigation of some of the major problems of the coming half-century, such as virus diseases, atheroma, hypertension, rheumatic disorders, and cancer, is lucid and readable; but the first volume may ultimately be more important, with its account of the activities of research institutes and the organization of work within them. Almost every facet of the complex that makes for medical advance is examined in a study which has been in process for fifteen years and may have as much influence on American medical research as Flexner's reports of forty years ago had on American medical education.

The great discoveries often come from observing the significance of some unexpected finding, which turns up in the pursuit of some apparently commonplace inquiry. The chance observation of glycosuria in depancreatized dogs led to insulin, the accidental fogging of a photographic plate gave us x-rays, and the initial discovery of penicillin was the result of chance acting on "the prepared mind." Hence the danger, to which Wiggers calls attention, of research "by proxy," in which technicians and junior assistants do the laboratory work. Wiggers says that at least three Nobel laureates did their own technical work with their own hands. It is only the inspired investigator, with a feeling for finer detail, who is likely to perceive the potential interest of the unexpected laboratory finding. Gauss, when he was once asked how he had become the greatest contributor to mathematical thought, answered simply, "By thinking about it all the time."

The growth of teamwork, so necessary in the use of our increasingly complex technologies, brings its additional problems. There are the difficulties of integrating into a medical team scientists who may not have had even a biological training and are apt to be baffled by the vagaries of living patients and their diseases. Again, such may be the difficulties of resolving jealousies between members of the team, and of making use of the total brain power of the group, that successful leadership is often as much an exercise in social and personal relationships as it is in science.

*From an Editorial in the *Lancet* Jan. 7, 1956.

The American writers make a strong plea for the promotion of fundamental as opposed to applied research—a plea the more necessary because problems of immediate importance are more likely to appeal to the laity, who in one way or another must foot the bill. It is curious that in the United States, the wealthiest country in the world, medical schools seem to have financial trouble as great as or greater than our own. At least half of them are said to have budget deficiencies, or to need large sums to keep up their standards; and yet there are immensely wealthy foundations in a position to spend money on a lavish scale. (Perhaps it is not entirely fortuitous that, since these volumes are written, the Ford Foundation has announced its intention to make a grant of 500 million dollars to the American medical schools and associated institutions.) Sometimes, of course, the money given by the public can be used only in some specific direction, such as cancer, psychiatry, and poliomyelitis; and the public does not necessarily give most generously to the most necessary purposes.

During years of intimate contact with investigators, research foundations become more sensitive to actual scientific possibilities; but unfortunately they do not pool their experience, and one after another they spend eight, ten, or more years in finding out the disparity between paper planning and actual needs. Some of the bodies financing research are apt to think in terms of immediate practical return for money spent; but others, of which the Markel Foundation gets special commendation, concentrate on helping promising men to enter the academic field.

The pattern of research is influenced also through direction of government funds, state and Federal. The richer states can afford to give their state universities greater freedom, but others insist to a greater or less extent on using the university as a "local service station." Thus in the dairy state of Wisconsin about two-thirds of the problems under study are connected in some way with the economic needs of the state; an example is the study of enzymes concerned with the ripening of cheese. To suggest that such applied research is not fruitful would be wrong; it has led, for instance, to the understanding of sweet-clover disease of cattle which had caused bleeding and death of whole herds, and from this to the trial of dicoumarol as an anticoagulant in medicine. Indeed, direct governmental interference in research has led to many excellent advances. On the other hand, control by politicians has obvious dangers.

America has immense resources, technical and intellectual as well as financial. Research is done in university medical schools and allied institutes like the Massachusetts Institute of Technology, under various Foundations (some with their own independent institutes, like the Rockefeller), in self-supporting clinics like the Mayo, in the pharmaceutical and chemical industries, and under the ægis of scientific societies and voluntary health organizations. In spite of unevenness and difficulties of integration, medical research proceeds in an immense productive flood.

—*I. S. Ravdin.*

Cancer and Common Sense

"All that is necessary for the triumph
of evil is that good men do nothing."
—Edmund Burke.

On reading the book *Cancer and Common Sense,* by Dr. George Crile, Jr., one experiences mixed emotions. Appreciation and admiration of the author for his scholarship and his warm sympathy for his patients, the true mark of the good physician, were increased. On the other hand, he has seized upon many unusual and bizarre features of the natural history of cancer and its treatment for the development of his thesis, and from these exceptions has expanded a philosophy for the cancer patient which is iconoclastic and dangerous. At the request of the American College of Surgeons, and as part of the semicentennial celebration of its founding, we recently have written a comparable monograph on cancer entitled *Fifty Years of Cancer Surgery.* In reviewing the amazing progress in cancer control, prevention, diagnosis, and treatment during this period we are so encouraged as to deny categorically most of Dr. Crile's pessimistic allegations.

The American Cancer Society, which is our chief educational agency, does not foster propaganda of fear. The public now is being educated in the facts about cancer. The informed are not so frightened as the ignorant. During the past quarter of a century it is now observed that patients often accept the diagnosis of cancer with some measure of equanimity, whereas in earlier years the pronouncement of cancer was avoided for fear of suicide, hysteria, or acceptance of inevitable death without treatment. The American Cancer Society has wielded the sword of knowledge rather than the weapon of fear.

In his introductory paragraph the author extols the resignation to death of the elderly woman of Bonifacio as she sat on the island mountain top, content in her ignorance of the fatal disease which inhabited her. Death comes to every man once, but it is to be hoped that he wishes to avoid or postpone it and is encouraged by the aid of his physician with all his skills and knowledge. If all physicians held such an unhealthly nihilistic viewpoint about treatment, how little incentive to progress would obtain. One sometimes sees parents accept a resignation to death of a minor child and deny it treatment for a cancer that might have been curable. Can one accept this as rational behavior? This philosophy is in accordance with the one which the skeptical Shakespeare phrased (with tongue in cheek): "Why, he that cuts off twenty years of life, cuts off so many years of fearing death."

"Cancer is a disease that does not always remedy itself. . . ." "There are harmless infections that are self-limited, or may disappear. The same is true of cancer." These quotations from the author's foreword and first chapter are supported by the recital of some collected instances of the spontaneous disappearance of cancers. The first quotation listed here is the understatement

of the year. In an experience of thirty years I have witnessed only two instances of spontaneous cure: in both patients small facial skin cancers disappeared after severe erysipelas. Such undue emphasis on the benignity and spontaneous recession of cancers in a book ostensibly written for the lay public without explaining the extraordinary rarity of such occurrences can do incalculable harm by encouraging the patient to procrastinate.

"In most cases a few weeks and in some even a few months or years of delay make no appreciable difference." Every physician is aware of the occasional cancer of the thyroid and breast which may be cured by local excision and of other bizarre and unpredictable behavior of cancers, which defy prediction and explanation. But to seize upon these rarities as an excuse for procrastination in treatment or conservative therapy generally applied is inviting disaster for the average patient with the average cancer. Every physician also is aware of the importance of the "cancer type" and that indefinable "host-tumor relationship" which plays such an important prognostic role in every patient from the incipiency of the cancer; that is, in the disparate behavior of the almost inevitably fatal inflammatory cancer of the breast with no host resistance, and the scirrhous breast carcinoma wherein the desmoplastic diathesis of the host exercises growth restraint by an enveloping fibrous dysplasia. One cannot compare different types of cancer and their natural history as an example on which to base the choice of treatment, but instead to apply what is defined as adequate therapy for every cancer as early as possible. The earliest adequate treatment for the most favorable cancer should improve the end results.

It is so easy to subtend wrong conclusions from evidence at hand. For example, in the case of bone sarcomas, patients with the shortest history have the worst prognosis. Explanation of this paradox lies in the fact that the less malignant, more slowly growing sarcomas of bone do not excite or warn the patient.

Dr. Crile accepts the application of so-called radical surgery in the treatment of cancer as a noble experiment from which we may withdraw gracefully when we recognize the futility of its application. Although admittedly the cure rate is inversely proportional to the radicality of the operations, it should be mentioned here that the patients treated by these ultraradical procedures could not be salvaged by orthodox methods. In my experience the greatest criticism of the radical surgery I have performed for advanced cancer has come not from general practitioners, nor from patients, nor even from relatives of patients for whom the therapy failed, but from other surgeons who seek a defense, an apology, and an excuse for not doing it.

Nevertheless, Dr. Crile should be thanked for a provocative, thoughtful essay with just enough truths to be factual, and just enough exaggerations to be argumentative.

—*George T. Pack.*

Pitfalls in Surgical Diagnosis

"O Thou who didst with pitfall and with gin
Beset the path I was to wander in,
Thou wilst not with predestination round
Enmesh me, and impute my fall to sin."

—*Omar Khayam.*

I had the good fortune to spend four years of the Second World War in Africa, as surgical adviser to the two decisive campaigns of that war, the capture of Abyssinia and the sweep across the Western Desert. Africa has a unique fascination. It is the oldest of the continents. It stood above the waste of waters when the rest of the world was submerged. It is so old that it is worked out and washed out, and little remains of its surface but miles of sand and rock, or of its structure but the heavy metals and the indestructible diamond. An American pilot whom I met in the bar at Shepheard's sipping a vodka and tomato juice described Africa, as seen from the air, as "millions of miles of damn-all." You can fly from the Mediterranean to the Indian Ocean and from the Red Sea to the Atlantic without seeing anything that would support even a camel for very long.

Africa is also the cradle of the human race, and the African is just emerging from the cradle, but being urged to walk before he has learned to toddle. He remains a cheerful, patient, musical, grown-up child, with a wonderful sense of humor and an unparalleled genius for idleness. His great problem is protein shortage. For many years his needs were supplied by raids on neighboring tribes, or by the fortunate arrival of explorers or other visitors. Now that missionaries are off the menu he must turn to animals, particularly the larger ones who supply more protein with less trouble, and he hunts them with great ingenuity and tremendous patience.

A pitfall is his device for trapping game, usually big game, and particularly elephants. A deep pit is dug in one of the game tracks, stout-pointed stakes are planted in the floor of the pit, the mouth is roofed with bamboos, covered by a layer of grass, then by earth on top of the grass, and the surface is made to look as much like the undisturbed section of the track as possible. By and by, an unsuspecting elephant comes along, crashes through to be impaled on the stakes below, and dies a lingering and painful death or is dispatched by the hunters when they come to inspect their trap.

A diagnostic pitfall is not quite the same thing. The trap is not set by the hunter, and the sufferer is not the man who falls into it, but his patient. The similarity lies in the fact that the trap is set in a well-known pathway, one whose landmarks should be so familiar that any divergence from their usual grouping should attract attention, and that carelessness, overconfidence, and neglect of the usual precautions, rather than ignorance, are the causes of the victim's downfall.

A diagnostic pitfall is a familiar problem set in an unfamiliar guise, that is, with some of the familiar features missing or with some unfamiliar ones added,

but yet bearing such indications of its origin that the man who approaches it with an open mind, who investigates carefully and who, having given to each fact in the history and the symptoms its appropriate weight, will make the right diagnosis. To miss the import of a clinical picture that is wholly atypical, the disease so rare that the specialist encounters it only half a dozen times in a lifetime, these are not mistakes. To make a wrong diagnosis, even, is no mistake provided that we have listened patiently, examined carefully, and pondered long and deeply.

The first essential in avoiding pitfalls, then, is constant watchfulness to recognize departures from the familiar picture. What is the familiar picture of disease? In every case it is compounded of two elements, the features of the disease itself and the features of the particular individual who is attacked. In collecting our facts we must keep these two aspects of the clinical picture constantly in mind; in assessing them and forming our conclusions we must apply a sixth sense—clinical wisdom—a personal quality built on the experience of similar cases in the past.

Cancer, if recognized early, is in most cases curable. The textbook picture of cancer is the picture of a disease many months too late for treatment. The pre-textbook picture is recognized only by the man who watches his fellows with the constant suspicion of a secret agent in enemy country, who moves among them with the alert mistrust of the jungle animal.

To fall into a pitfall is humiliating to the surgeon, but it may be disastrous to his patient. Surgery is the art of treatment by doing something, and, to be effective, that something must be done at the right time. In medicine, we can usually wait till the diagnosis is clear. In surgery, if we wait too long, it may be only too clear. Surgical diagnosis may, in some cases, be little more than intelligent anticipation as a basis for action.

Can we lay our finger on the common causes of error? First I would put a failure to recognize the normal. We should all know our normal anatomy, but how many of us are really familiar with the normal appearance of parts not often seen, with the normal feel of parts we seldom palpate until they are diseased, with the variations in the normal from individual to individual and with the changes in the normal that come with advancing years?

Second, we make mistakes in taking short cuts. There is much sense in a saying of the Professor of Surgery in Cape Town, Charles Saint: "A spot diagnosis is the quickest way to reach the wrong conclusion."

Last, we make mistakes by not looking at the patient as a whole. Many lesions that seem at first to be local are really symptoms of a general disease. The tabetic joint is a familiar pitfall. Another is the patient with a large liver and a glass eye, the eye having been removed in childhood for a melanotic tumor. Both these pitfalls should safely be crossed by the man who looks at the whole patient.

It is our privilege to learn from the mistakes of others. On our journeys along the well-known pathways of surgery we come across a number of traps into which our friends have fallen, now revealed as gaping holes with crumbling walls, the beams that supported the concealing covering exposed to our gaze.

How do we avoid falling into the next one we meet? Come with me to Africa and look at the elephant in his native haunts. There is a herd making their leisurely way through the bush. They can barely be seen for they have rolled in the mud of every pool they have passed and they are the color of their surroundings. Nearest to us is the old bull who is responsible for their safety. As he feeds, his head is turning this way and that, his trunk is sniffing the breezes, his ears are catching every sound, and his little pig eyes are darting their glances in every direction. In spite of our caution we have alarmed him, for his enormous ears are suddenly spread out like sails, he sounds a shrill trumpet of warning, and he lumbers off.

We human beings have bought our intellectual supremacy by the development of manual dexterity combined with binocular vision, and in doing so we have abandoned our jaws as weapons of defense and our noses as instruments of defense. But we can still stop and look and listen. Every surgical diagnosis is an exploration into unknown territory. We can never say: "We have been this way before," only: "We have been along a similar path before." Are all the landmarks the same? They may be, but are we sure?

The price of safety is eternal vigilance.

—*Sir Heneage Ogilvie.*

Notice

Because of the large number of original communications awaiting publication in SURGERY, case reports are no longer being accepted.

—THE EDITORS.

Appraisal of Progress in Surgical Therapy

CONDUCTED BY WARREN H. COLE, M.D.

MALIGNANT MELANOMA—THE IMPORTANCE OF EARLY AGGRESSIVE TREATMENT

HERBERT WILLY MEYER, M.D., RANCHO SANTE FE, CALIF.

(From the Tumor Service of the Department of Surgery, New York University, Post-Graduate Medical School)*

THERE is only one efficient method of treatment for malignant melanoma. This is adequate radical surgery expertly performed. Unfortunately, many physicians and some dermatologists, who are frequently the first clinicians to see these cases, do not look upon malignant melanoma with sufficient caution and seriousness. Likewise, there are also many surgeons who do not look upon the lesion of malignant melanoma with sufficient fear and respect. The prognosis is always so grave that special principles and techniques of therapy are required, quite different from the techniques which may be adequate for nonmalignant surgery.

Melanoma is a vicious disease. It quickly takes the lives of apparently healthy people, frequently young people who otherwise seem to be in perfect health, were it not for their small lesion of malignant melanoma. It is possible that they may be dead within a few months of the time that they are first seen. Their ending may indeed be most tragic.

Clinically there are two groups of malignant melanomas. The one group composes the fulminant cases in which the melanoma cells spread throughout the body from the primary site by way of the blood stream. Metastases quickly riddle the body. At the present time there is no method of therapy that will prolong the lives of these unfortunates. Chemotherapy may, in the future, offer some faint hope of relief. The prognosis in these cases is almost hopeless.

The other malignant melanoma cases are of the nonfulminant type. In these the melanoma cells may spread at first by direct extension into the surrounding tissues. Sometimes the cells skip a small immediate area around the margin of the primary lesion and first reappear a centimeter or more away. This skip area frequently gives the appearance of a halo on inspection. This occurrence is one of the main reasons why a very wide excision of the primary lesion is always indicated. Besides the spread by direct extension the

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*The author was formerly Chief of the Tumor Service.

melanoma cells may pass into the superficial lymphatic vessels. At times they also enter the deeper lymphatic vessels. The malignant cells then drain into the regional lymph nodes. Here they are held in check for shorter or longer periods of time before they pass further and enter the blood stream and then quickly cause distant metastases. It is in these nonfulminant cases that the surgeon can salvage a goodly number of patients if he is fortunate enough to see the patient early in the disease. It is this type that we wish to discuss, because the surgeon can actually do something for the patient.

Unfortunately, at the moment there is no method by which we can definitely tell whether we are dealing with a fulminant type or a nonfulminant type of case. Therefore it is our duty to give these patients at least the benefit of the doubt and to consider them to belong to the more favorable, nonfulminant group unless there is actual evidence clinically or by laboratory examination that they already have fallen into the fulminant group on account of distant metastases.

Melanomas may occur anywhere in the body. However, they are more apt to develop in a junction type of nevus on the dermal surface of the body. They are especially prone to occur along mucocutaneous margins, i.e., the genitals and anus and on the extremities such as the soles of the feet, toes, subungual regions, palms of the hands, fingers, and on the trunk and head or neck. They comprise only 1 to 2 per cent of all malignancies, but they form about 20 per cent of all skin cancers. The prognosis is especially poor when they develop during pregnancy. In children, the lesions histologically look like malignant melanoma but clinically they rarely metastasize, and therefore they can be treated more conservatively. Melanomas occasionally occur in the oral cavity, the gastrointestinal tract, and the eye. In these locations they must be handled like any other type of malignancy.

A wise method of therapy is the prevention of the possible development of melanoma. This entails the surgical excision of nevi that are located in areas of the body where they are under constant or frequent irritation. These areas are especially those around the waist, genitals, extremities, face, shoulders, etc. It is always good advice to suggest the preventive removal of such nevi. This is especially so if the clinician is suspicious that the nevus may be of the junction type.

There are certain changes that may occur in nevi of many years standing, which should make one suspicious that malignant melanoma may be developing. They are: (1) any sign of activity or increase in size; (2) change in color; (3) pain, itching, irritation, or discomfort in nevus; (4) infection; (5) bleeding, ulceration, or crusting.

The correct diagnosis can only be made by histologic examination. This means a biopsy and a fixed section examination. It is never wise to rely on a frozen section diagnosis in melanoma and no major surgical procedure should be contemplated on this type of diagnosis. The suspicious melanoma lesion should never be "cut into" by either incision or by punch biopsy. The biopsy must always be a wide excision biopsy.

Therefore, the treatment of melanoma is efficient, adequate, radical surgery.

The following various methods of treatment should be avoided: the cautery, desiccation, electric needle, carbon dioxide snow, caustics, pastes, chemicals, or the like.

It is my opinion that ultraradical surgery such as quarterectomy of either the upper shoulder girdle or of the lower extremity is not indicated in the treatment of melanoma at the present time, except in a very few exceptional circumstances. Therefore, we shall not enter the present controversial discussion between adequate radical surgery and ultraradical surgery.

I shall describe my idea of the standard adequate radical procedures in the various areas of dermal melanomas. I think that the majority of surgeons at the present time adhere to these principles. I am convinced that the basic principle of all cancer surgery applies to melanoma as it does to all other forms of malignant disease. It demands the wide excision of the area of the primary lesion in continuity with the regional lymphatic area. This principle should be followed whenever it is technically feasible.

There are certain circumstances, however, when only wide excision should be the method of procedure. This may be the case if the lesion is extremely small and histologically very superficial and noninfiltrating. One occasionally may see such a case when a very early melanoma develops superficially in just one area of a junction-type nevus. The surgical pathologist may offer the opinion that the lesion is early, superficial, noninfiltrating and has been completely excised. At times the pathologist even goes so far as to say that no further surgery is indicated. I personally am always somewhat anxious about such advice and do not adhere to such advice without most careful study of the individual case, the microscopic section, and consultation with the surgical pathologist. Basically in melanoma I favor wide excision in all directions and a regional lymph node dissection in almost every instance. I have seen minute, scattered, single-cell melanoma metastases in the regional lymph nodes, even in the early superficial case of melanoma, when careful study of the excised nodes in a preventive node dissection has been performed. These nodes were clinically not palpable. In such instances it *must* be of benefit to the patient that such nodes, with these early metastases, be removed from the body rather than left there until the metastatic tumor has grown so large that it can be diagnosed by physical examination. During the time that these nodes are enlarging, so that they can finally be diagnosed, they must be a constant focus from which further metastases can and will occur. Melanoma is a vicious disease and we must look upon it with the greatest respect and fear. The fact that lymph nodes are clinically not palpable does not mean that metastases are not already present. To wait till the nodes are so large that they become easily palpable means to wait till the disease is already far advanced, and the prognosis becomes very grave. The chance of arrest and salvage of the patient is greatly reduced. I cannot follow this philosophy. Merely to perform a wide excision and then await the evidence of node metastasis and follow this with an aspiration biopsy or excision of a node for positive

diagnosis does not seem logical to me. To follow this late positive diagnosis of node metastasis with amputation of the node area by a quarterectomy rather than a node dissection is certainly a far more mutilating procedure. Unless the late results show better salvage rates than we have found in our cases, we will not advise such ultraradical surgery.

In far-advanced cases with evidence of distant metastases it may be advisable to suggest only wide local excision without node dissection. There are, of course, also instances where the patient will refuse permission to perform node dissection although the surgeon will have tried his best to urge the patient to permit such a procedure.

There are also times when a surgeon sees a patient in consultation after another physician has removed a melanoma by a small excision. It is always important to obtain the slide by which the diagnosis of melanoma was made, and the surgeon who was consulted should review this slide with his own surgical pathologist. In conference with him he must decide what further procedure is indicated. In such instances the consulting surgeon, who has had experience with these types of cases, will feel that a further excision, wider and deeper than the original one, is indicated. As a general rule, the excisions should be approximately 4 to 5 cm. from the margin of the primary lesion. In most instances a skin graft will be necessary to close the resulting defect. Occasionally in some areas of the body, especially if the primary lesion is very small, a closure of the wound by suture without graft may be feasible.

Every effort should be made at the time of excision of the lesion to avoid possible tumor embolization. Local anesthesia, which distends the tissues and causes local pressure changes, should be avoided. Biopsy in suspicious melanoma cases should never be an office procedure. Free bleeding from the specimen side should be permitted. Sharp hooks or rakes should never be used on the tumor side. Silk sutures placed at the skin margin of the specimen are employed for retraction and are very satisfactory. Gentleness, I repeat gentleness, in handling tissues is the ever-constant watchword of good surgery. May I refer at this moment to the splendid editorial by Sir Heneage Ogilvie?[4] It emphasizes so well the great importance of this fact. Lauren Ackerman's article[1] on the implantation of tumor cells during surgery also makes this point. Warren Cole and many other surgeons have preached this philosophy. We have taught it at the old New York Skin and Cancer Hospital for many decades.

Whenever operation in continuity is not feasible, then stage operations become necessary. This applies especially to the primary lesions of melanoma which are situated on the distal portions of the extremities. Here wide local excision or local amputation of digits is indicated. If regional lymph nodes are not palpable clinically, we usually wait three to four weeks between the primary excision of the melanoma and the regional node dissection. This time interval allows melanoma cells on their way to the lymph nodes to drain into them. If nodes are palpable clinically, then the time interval between procedures is only ten to fourteen days. In some clinics it is felt that the

node dissection should be performed at the same time as the excision of the primary lesion. Whenever operation in continuity is not feasible, I personally feel it is better not to block the normal flow of the lymph stream at the time of the excision of the primary melanoma. Sometimes the primary lesion is so situated that it becomes necessary to dissect more than one regional lymph node group.

Lesions of the head and face can frequently be removed in continuity with the cervical lymphatics. If this is impossible, secondary radical cervical node dissection must be performed. In melanoma it is always indicated to excise the sternomastoid muscle as well as the internal jugular vein. Careful, meticulous dissection of all the nodes that lie along the anterior border of the trapezius in the posterior triangle of the neck is especially important. I have seen late metastases in just this region following an incomplete radical cervical node dissection.

Lesions on the hands and forearm require excision of the epitrochlear node area and an axillary node dissection. A large curved incision with a wide base starting at the insertion of the pectoralis major at the humerus and extending downward along the free border of the pectoralis at the axilla and then down onto the chest wall in the axillary line gives excellent access. When indicated, a further incision from the apex of this flap at mid-axilla upward to the clavicle gives additional better exposure of the axillary contents. If enlarged nodes are not seen or palpated, it may be possible only to retract the pectoralis major and minor muscles. This procedure frequently gives adequate access to the apex of the axilla. If nodes are present, better access is required. Then the pectoralis major and minor muscles may be cut across at right angles from their free border to the clavicle. They need not be resutured at the end of the procedure. Another procedure, which I prefer, which gives excellent exposure of the axillary contents, is excision of the axillary portion of the pectoralis major and minor muscles together with the axillary dissection. If many nodes are found, I also excise the axillary vein, making every effort to preserve the cephalic vein and its junction with the axillary vein. Edema of the arm will not ensue and function of the arm is excellent.

The complete groin dissection with removal of the femoral, inguinal, and deep iliac lymph nodes is best accomplished according to a technique we have employed at the Tumor Clinic of New York University, Post-Graduate Medical School. This procedure has recently been described by Gumport and me.[2] In this procedure one or sometimes both recti muscles are transversely divided just above their insertion into the symphysis pubis. The sartorius muscle is also divided just below its origin at the anterior superior spine of the ilium. By preserving its nerve and blood supply the muscle is later rotated or moved mesially to cover the exposed femoral artery, vein, and nerve. It fills in the marked hollow that is present after the node dissection. Healing is much improved.

In the axillary, cervical, and groin dissection a catheter or catheters with lateral holes are placed in the wound and connected with a suction pump (electric) or a Wangensteen suction apparatus. This prevents the collection of blood, serum, or air. The skin flaps quickly become adherent to the underlying structures. Quicker and better healing with less chance of marginal skin necrosis is provided.

The results in 153 proved cases of melanoma seen and followed at the Tumor Clinic of New York University, Post-Graduate Medical School are given here in brief.* These cases have been followed for one to five or more years. Of the 153 patients, 91 (59 per cent) are alive and 62 (41 per cent) are dead. Of 107 patients who have been followed for a period of five or more years, 54 (51 per cent) are alive and 53 (49 per cent) are dead. Fifteen patients were lost to follow-up and these are considered dead from melanoma. In 64 of these 107 cases, regional node dissections were performed; 34 patients (53 per cent) are alive five years or more and 30 (47 per cent) are dead. In 28 of these 64 patients the lymph nodes examined were negative; 20 (71 per cent) are alive and 8 (29 per cent) are dead. In 36 of these 64 patients the nodes were reported as positive with metastases; 14 (39 per cent) are alive five years or more and 22 (61 per cent) are dead. Clinically in 29 sets of nodes dissected the nodes were considered negative before operation. In 8 of these cases the nodes were reported positive on histologic examination. This is an error in diagnosis of 28 per cent. If serial sections had been made of these nodes, it is possible that more positive nodes might have been found. In 37 sets of nodes diagnosed as positive for metastases before operation, 8 cases were reported negative, an error of 22 per cent. There were 43 patients in whom no node dissection was performed for one reason or another as discussed above. Of these, 20 (47 per cent) are alive and 23 (53 per cent) are dead.

SUMMARY

The results we have obtained in this dread disease have led us to believe that the principles, policies, and philosophy described above are the wise ones to follow in the treatment of melanoma. Aggressive treatment by adequate radical surgery should be continued to be taught and followed. I am of the opinion also that preventive lymph node dissection should be performed whenever possible, even previous to clinical evidence of metastases, certainly as early in the course of the disease as possible.

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*The statistics have been compiled and the patients followed by Dr. Stephen L. Gumport of the Tumor Service. I was formerly Chief of this service, until April, 1955, and I am indebted to Dr. Gumport for his permission to make use of these figures at this time.

Reappraisal

CONDUCTED BY CLARENCE DENNIS, M.D. ASSISTED BY ALFRED HURWITZ, M.D.

INTRODUCTION

OPERATIONS employed for the treatment of peptic ulcer have shown ebbs and tides of popularity. None, not even the standard three-quarter subtotal gastrectomy, has proved to be so efficacious as to remain unchallenged. The postoperative complications that have appeared in an appreciable number of patients include the development of recurrent or marginal ulcers, the dumping syndrome, inability to gain weight due to faulty digestion of fats and protein, and anemia. At the present time there is a growing wave of enthusiasm for the performance of a Billroth I instead of a Billroth II procedure and for the removal of not more than 50 per cent of the stomach combined with subdiaphragmatic vagotomy. Only time will tell whether these procedures will be followed by a lower incidence of complications than is presently manifest after the performance of a standard three-quarter resection of the stomach and gastrojejunostomy. The experience of three different investigators with these operations is recorded in the following brief papers.

GASTRIC RESECTION FOR PEPTIC ULCER; BILLROTH I VERSUS BILLROTH II

STEN WALLENSTEN, M.D., STOCKHOLM, SWEDEN

(From the Surgical Department, Kungl. Serafimerlasarettet)*

IN 1953 the author, in association with Dr. Lars Göthman, published in SURGERY† an article entitled: "An Evaluation of the Billroth I Operation for Peptic Ulcer." It was then reported that the results obtained with this operation in ulcer cases were good and compared favorably with the results obtained with other partial gastrectomy techniques as evidenced in previously published reports.

Such an investigation does not reveal all the advantages and disadvantages unless comparison can be made with similar material where another type of operation has been employed—and preferably the Billroth II. Accordingly, a further follow-up examination was undertaken with the purpose of making such a comparison.

*Head: J. Adams-Ray M.D., Professor of Surgery pro tem., Karolinska Institutet Medical School, Stockholm.

†Volume 33, No. 1, January, 1953.

In the assessment of the results of such an operation in the past, a series has usually been made by the rather stereotyped procedure of grouping the cases according to the success of the operation. This method inevitably involved a subjective factor of selection. In the present study the sole criteria were postoperative conditions which could be recorded objectively, and thus represented numerically.

Comparison was made of two series of peptic ulcer cases in which the Billroth I and II techniques were used. In the latter, Polya's operation was performed. The Billroth I material of 363 cases was from the Surgical Department of Falu lasarett, where this type of operation is the routine method for the surgical treatment of peptic ulcers. The 893 cases comprising the Billroth II material were treated at the Surgical Department of the Serafimerlasarett, where this was the usual method.

The immediate postoperative results were largely the same for the two types of operation. To study the late results, from each series those cases were selected that were treated by the chief surgeons. This procedure excluded varying personal factors in the performance of both operations and at the same time ensured material that had been treated by very experienced surgeons. The level of resection was the same in both groups.

All operations were performed from 1932 to 1949. The shortest observation time was four years. The total material comprised 675 cases, 248 of them B I and 427 B II. After excluding patients who had died from the operation and during the observation period and those who could not be traced, there remained for follow-up examination 204 B I and 347 B II cases. Of these, 202 B I (99 per cent) and 322 B II (93 per cent) presented themselves, the majority of the patients being examined personally by the author. The examination was centered on (a) new ulcers in the stomach, duodenum, and the anastomosis; (b) anemia and sideropenia; (c) postcibal symptoms; and (d) changes in weight in relation to the preoperative weight.

Recurrences.—

	BILLROTH I			BILLROTH II		
	NO. OF OPERATIONS	RECURRENCES		NO. OF OPERATIONS	RECURRENCES	
		NO.	PER CENT		NO.	PER CENT
Men						
Gastric ulcer	33	2	6.1	46	0	0
Duodenal ulcer	111	13	11.7	190	8	4.2
Women	59	2	3.4	86	0	0

For the male patients the frequencies of recurrence relating to the B I and B II operations for gastric ulcers were 6.1 and 0 per cent, respectively. The difference was not statistically significant. For the duodenal ulcers, on the other hand, the difference was more significant, the figures for the B I and B II being 11.7 and 4.2 per cent, respectively. In the female patients there was no statistically significant difference in the frequency of recurrence for the two types of operation.

Most of the recurrences were during the first six to seven years after the operation. To assess the prognosis with respect to the possibility of no recurrence after the two types of operation, use was made of the mathematical procedure applied by McWhirter in 1948 for a similar calculation relating to cancer of the breast. The prognosis curves obtained are given in Fig. 1.

Postoperative Anemia and Sideropenia.—Anemia was diagnosed on the basis of the hemoglobin values: Males 13.6 Gm. per cent; females < 11.5 Gm. per cent. Sideropenia was diagnosed when the serum iron was below 60 γ per cent; both anemia and sideropenia were found to occur commonly after partial gastrectomy. It was also found that the B I operation gave a significantly lower frequency of anemia than B II. This was particularly so in the case of the female patients. The frequencies of sideropenia and anemia were, of course, parallel, but some cases were found with only sideropenia.

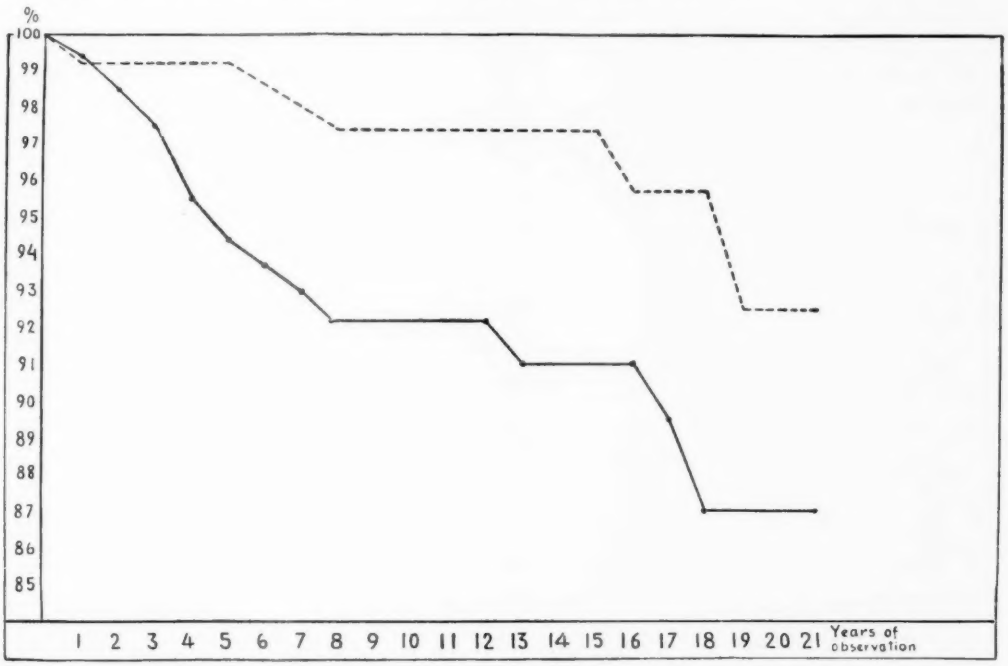

Fig. 1.—Incidence of freedom from recurrence of peptic ulcer after partial gastrectomy according to Billroth I and II methods. B I = ———, B II = – – – –.

Postoperative Postcibal Symptoms.—Pronounced manifestation of these symptoms was commoner after B II than after B I operations, the figures being 16.6 and 5.3 per cent, respectively. The difference is highly significant. There was also a pronounced difference with respect to sex, the higher figure being for the female patients.

Postoperative Weight Changes.—The weight at the follow-up examination was compared with the value prior to operation. Only differences of more than 5 kg. were recorded as definite changes in weight. There were certain losses in weight, judged on these criteria, in 5 per cent of the B I and 13 per cent of the B II cases.

SUMMARY

The comparative study showed that the B I operation had the disadvantage of a higher frequency of recurrence than the B II operation, in the case of duodenal ulcers in males. The advantages of the B I method include a lower frequency of postoperative anemia, of marked postcibal symptoms, and of postoperative losses of weight.

The main advantage of the B II method was a lower frequency of recurrence.

Our indications for the present concerning the two types of partial gastrectomy are: in men with duodenal ulcer, B II; in men with gastric ulcer, B I; in women, B I.

It seems as if the only disadvantage of the B I operation lies in the fact that, for male duodenal cases, there is definitely a higher frequency of recurrence. The wisest procedure, therefore, would be to perform vagotomy in these cases at the same time as the B I operation. We have no evidence that this combined method is superior to the B II operation, but it is hoped that we shall have material later which will enable a comparison to be made.

CONSERVATIVE GASTRIC RESECTION COMBINED WITH VAGOTOMY

REGINALD H. SMITHWICK, M.D., BOSTON, MASS.

I FEEL that the operation of vagotomy and gastroenterostomy is one which should be employed when the management of the duodenal stump would be difficult or hazardous and when the condition of the patient is such that the risk of gastric resection would be too great.

I believe that conservative gastric resection combined with vagotomy is the procedure of choice in the treatment of chronic duodenal ulcer.*

We remove the distal 50 per cent of the stomach including all of the antrum.

The complications following a conservative gastric resection and vagotomy are similar to those following subtotal gastrectomy alone. There is essentially no difference in the morbidity and the mortality following the two operations. The most serious complications following either operation are those related to the management of the duodenal stump. Two of three deaths following hemigastrectomy and vagotomy and three of five deaths following subtotal gastrectomy were due to this cause. Otherwise, the operative mortality in both series of patients would have been approximately 1 per cent. (Table I.)

Some recent follow-up data might be of interest. (Table I.)

The operative mortality in 190 patients treated by subtotal gastrectomy was 2.6 per cent and in 135 patients having hemigastrectomy and vagotomy was 2.2 per cent. The clinical results in 154 patients followed 1 to 6 years after subtotal gastrectomy were excellent in 23 per cent, good in 41 per cent, fair in 24 per cent, and poor in 12 per cent. Comparable figures for 56 patients

*Farmer, D. A., and Smithwick, R. H.: Hemigastrectomy Combined With Resection of Vagus Nerves, New England J. Med. 247: 1017-1022, 1952.

following hemigastrectomy and vagotomy were 41 per cent, 46 per cent, 9 per cent and 4 per cent indicating a much higher percentage of excellent results and a much lower percentage of fair and poor results in patients having the combined procedure. To date there are already 18 patients in the subtotal gastrectomy series who have proved or suspected gastrojejunal ulcers. In 3 patients (2 per cent) a gastrojejunal ulcer has been demonstrated, and in 15 patients (10 per cent) it is suspected. There are no either proved or suspected gastrojejunal ulcers following the combined procedure. We feel that any patient who has free hydrochloric acid following an operation for duodenal ulcer can develop a recurrent ulcer. While it is true that many patients who do have free hydrochloric acid following operations of one sort or another never do develop gastrojejunal ulcer, nobody knows which patient will do so.

TABLE I

OPERATION	NO. OF CASES	OPERATIVE MORTALITY	CLINICAL RESULTS (1-6 YEARS)				GASTRO-JEJUNAL ULCER	
			EXCELLENT	GOOD	FAIR	POOR	PROVED	SUSPECTED
Hemigastrectomy + Vagotomy	135	2.2%	41%	46%	9%	4%	0	0
Subtotal Gastrectomy	190	2.6%	23%	41%	24%	12%	3	15

The only thing that seems absolutely clear is that if a patient has no free hydrochloric acid when fasting and when stimulated by food or insulin that he will not have recurrent ulcer disease. Consequently, we are interested in an operation which produces a high incidence of achlorhydria. (Table II.)

TABLE II

TIME POSTOPERATIVE	HEMIGASTRECTOMY + VAGOTOMY		SUBTOTAL GASTRECTOMY	
	NO. OF CASES	PER CENT WITH FREE HCL	NO. OF CASES	PER CENT WITH FREE HCL
8 days-23 mo.	87	14	76	36
24-70 mo.	28	4	102	39
Totals	115	11	182	37

Following subtotal gastrectomy 37 per cent of 182 patients carefully followed still have free hydrochloric acid, whereas 11 per cent of 115 patients have free hydrochloric acid following hemigastrectomy combined with vagotomy. It is interesting also to know that with the passage of time the percentage of patients with achlorhydria following subtotal gastrectomy appears to be decreasing slightly whereas it appears to be increasing following the combined operation. Thirty-nine per cent of the patients studied 2 years or more after subtotal gastrectomy have free hydrochloric acid whereas 4 per cent of those followed 2 years or more have free hydrochloric acid following the combined maneuver. Therefore, at the present time, both on the basis of clinical results and on the basis of secretory data the combined operation appears to be superior to subtotal gastrectomy.

Seventy-five per cent of the patients that we have studied following posterior gastroenterostomy and vagotomy have free hydrochloric acid postoperatively, and we believe that with the passage of time the incidence of recurrent ulceration in this group of patients will be high. In general we prefer the Billroth II type of anastomosis with a comparatively short loop anterior gastrojejunostomy. We believe it is the simplest technique and the safest for most surgeons. We have had almost no difficulty with nutrition following the combined operation with this type of anastomosis and only one incidence of dumping of any consequence. Other secondary untoward side effects have been much less common following the combined maneuver than after subtotal gastrectomy.

As time goes on we are becoming increasingly enthusiastic about the results of the combined procedure and are increasing the size of the series fairly rapidly at the present time since we believe that our present data indicates that the long-range outlook following the combined procedure is excellent and superior to that following any other operation that we have had experience with. We believe that the combined maneuver, conservative gastrectomy and vagotomy, most nearly satisfies the two major objectives of surgery for duodenal ulcer, namely, protection against recurrence of the disease and an extremely low incidence of untoward secondary side effects.

EFFICACY OF 40 PER CENT GASTRECTOMY COMBINED WITH VAGOTOMY FOR DUODENAL ULCER

L. W. Edwards, M.D., and J. L. Herrington, Jr., M.D.

Nashville, Tenn.

WE HAVE somewhat revised our position as expressed in 1953.* At the present time, we do not perform vagotomy and gastroenterostomy for the treatment of duodenal ulcer except in the occasional instance when a poor-risk, elderly patient is encountered in whom the risk of vagotomy and resection would be great. In our early experience we did perform vagotomy and gastroenterostomy in a series of approximately 40 patients; excellent results were obtained in only about 60 per cent of this small group.

As regards vagotomy and gastric resection, we are very enthusiastic about this operation at the present time. We perform vagotomy combined with a distal 40 per cent resection which completely removes the antral segment. We have personally performed this operation in over 200 patients and the results have been excellent. The patients have been followed carefully and there is not a single case of recurrent ulceration in the entire group. These patients have been followed from a few months up to 9 years. We feel that the extent of the resection need not be over 40 per cent when vagotomy is

*Edwards, L. W., and Herrington, J. L. Jr.: Vagotomy and Gastroenterostomy-Vagotomy and Conservative Gastrectomy, Ann. Surg. 137: 873-883, June, 1953.

added. In the vast majority of cases we remove the duodenal ulcer and resection is carried out to approximately the angularis on the lesser curvature and approximately midway on the greater curvature. This insures at least a 40 per cent distal resection and completely removes the antrum. These patients have no free fasting hydrochloric acid postoperatively, and also have an achlorhydria to a test meal and histamine stimulation. The patients who were operated upon 8 to 9 years ago still have an achlorhydria. Whenever possible, we prefer to establish continuity by a gastroduodenostomy (Billroth I) and feel this operation can be carried out in the majority of instances. Of course, there are some cases in which the ulcer is so adherent to the pancreas and surrounding structures that a Billroth II or one of its modifications is performed.

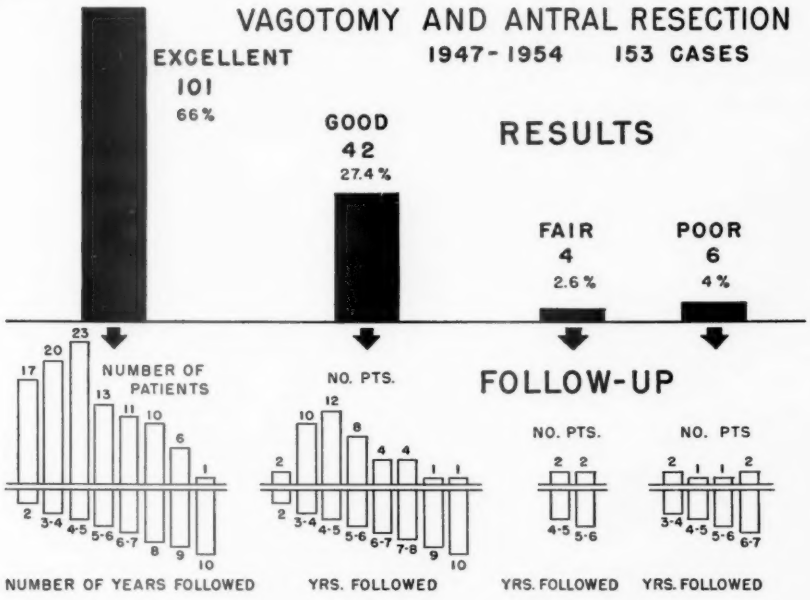

Fig. 1.—Results with vagotomy and antrectomy during the years 1947 through 1954. These patients have been followed for a minimum of 2 years up to almost 10 years. As recorded in the table, we have obtained excellent and good results in 93.4 per cent of this group. The 4 patients listed as fair results have no evidence of marginal ulcer but do have some dumping and vague abdominal complaints. In the 6 patients listed as poor results, each has been studied in great detail and there is no evidence suggesting a marginal ulcer. Two of these patients with severe dumping symptoms had had a Billroth II originally; both have been converted into a Billroth I and are now doing fine. The most significant information derived from this study shows that there has been no instance of marginal ulceration in this group of 153 patients.

The number of complications has been small in this group of patients. There have been two instances of duodenal stump leakage in those patients undergoing the vagotomy and Billroth II procedure, but both recovered. A few of the patients complained of some fullness during the immediate postoperative period, but this has not been a major problem. An occasional diarrhea is also noted, but in no instance has this been prolonged. As mentioned, there has been no instance of recurrent ulceration and we would imagine that dumping occurs to some extent in approximately 25 per cent of the entire group, but we have, at present, only three patients in whom dumping has been a serious problem. All three of the patients had Billroth II type of reconstruction.

One of these patients has recently been converted to a Billroth I operation with marked gain in weight and improvement in dumping. It is our distinct impression that dumping is less frequent following the Billroth I operation. Postoperative anemia has been encountered only rarely in this group of over approximately 200 patients.

At the present time, we no longer perform radical subtotal gastric resection for the treatment of duodenal ulcer, but feel that vagotomy combined with antral resection leaves the patient in a better nutritional state and produces less long-term postoperative sequelae than the former operation.

Announcement

On Feb. 14, 1957, the Buffalo Surgical Society will sponsor the Roswell Park Lecture, this year to be given by Dr. Alton Ochsner, Director of Surgery, Ochsner Clinic, New Orleans, La.

The title of this year's lecture will be "Bronchogenic Cancer: Factors Which Influence Long-Term Survival."

Dr. Ochsner will be awarded the Society's Gold Medal being given for the tenth time in honor of Dr. Roswell Park, Professor of Surgery, University of Buffalo, 1883-1914. Previous lecturers and recipients of the medal are as follows: Dr. Allan C. Whipple (1948), Dr. Evarts A. Graham (1949), Dr. Dallas B. Phemister (1950), Dr. Frederick A. Coller (1951), Dr. Edward D. Churchill (1952), Dr. Warren H. Cole (1953), Dr. I. S. Ravdin (1954), Dr. Alfred Blalock (1955), and Dr. Robert E. Gross (1956).

Book Reviews

CONDUCTED BY J. GARROTT ALLEN, M.D.

Modern Trends in Orthopedics. By Sir Harry Platt. (Second Series) New York, 1956, Paul B. Hoeber, Inc. Pp. 331.

To those who have had the opportunity to see the first series of these essays, the second collection needs no recommendation. This second series consists of a collection of eleven essays dealing with a variety of orthopedic subjects written by well-established English orthopedic surgeons. The essay on reconstructive surgery of the hip joint is especially outstanding. There are essays dealing with the treatment of tuberculosis, with peripheral nerve injuries, with contractures of the hand, with fractures of the neck of the femur, and displacements of the upper epiphysis of the femur and other subjects of interest to orthopedic specialists.

The material is concisely presented, well illustrated, and in an easily read form. This volume is a welcome addition to the orthopedic literature and can be read with interest and appreciation by all those surgeons dealing with orthopedic conditions.

—Leonard F. Peltier

Surgery of the Eye: Diseases. By Alston Callahan. Springfield, Ill., 1956, Charles C Thomas. Pp. 447, 263 ills. $25.00.

A surgeon reading a book concerning surgery can generally deduce after glancing at a few pages whether the book evolved from personal experience at the operating table or from literary study. This new book on ophthalmic surgery is obviously written by and intended for the surgeon in the operating room. It presents only those methods with which the author has had experience. There are excellent discussions of the basis for selection of the operative procedures, the techniques of the operation, and the management of the normal and complicated postoperative course. The first chapter discusses briefly but adequately the techniques and drugs used for local anesthesia about the eye. There is brief reference to general anesthetic techniques and the use of curare. The next five chapters present a comprehensive and beautifully illustrated discussion of surgery of the eyelids. Here the emphasis is upon those procedures most useful to the author with the reasons for his preference clearly stated. Single chapters are devoted to the lacrimal system, congenital anomalies, the conjunctiva and cornea, and the iris. Cataract is discussed in six chapters and glaucoma in five. The discussions concerning the complications of these latter two procedures are particularly well done. Single chapters are devoted to enucleation, muscle surgery, and surgery of the orbit. In this common ground of the neurosurgeon and eye surgeon, the emphasis is perhaps naturally ophthalmic—perhaps distressingly so from the viewpoint of the neurosurgeon. An appendix entitled "Advances in Management of Injuries of the Eye" concludes the text. This is an extension of the author's earlier book, *Surgery of the Eye: Injuries*, which has remained pre-eminent since its publication in 1950.

This new book seems certain to join the few standard reference books on surgery of the eye. It is believed that the general surgeon, particularly one working about the head, and the plastic surgeon will find many of the chapters of considerable interest. It may be recommended without hesitation to the ophthalmologist and his residents and to all surgeons whose work in surgery brings them near the eye and the eyelids.

—Frank W. Newell

Peripheral Vascular Disease. By Edgar V. Allen, Nelson W. Barker, and Edgar A. Hines. Ed. 2. Philadelphia, 1955, W. B. Saunders Company. Pp. 825, 316 ills.

This textbook is the result of collected contributions of thirteen members of the Staff of the Mayo Clinic, Rochester, Minnesota, all of whom have a major interest in vascular diseases. The first edition was published in 1946 and became an almost standard reference upon the subject. This original contribution is only outdone by the second edition.

The book is divided into three sections: the first is devoted to the definition of terms and the techniques of diagnosis; the second section is a series of classical descriptions of the disease states; the third section discusses the surgical management of the vascular diseases. The individual chapters are complete with a brief historical background of each topic and a very complete discussion of the pathophysiology and management. The bibliography is well outlined throughout.

I feel that this text is of great value for both the student and the specialist interested in this extremely wide field of medicine.

—Thomas O. Murphy

Operative Surgery. By Charles Rob and Rodney Smith. Vol. I. London, 1956, Butterworth & Co., Ltd. Price unstated.

This is the first of the 2-volume British presentation, designed to cover the fields of abdominal surgery exclusive of most aspects of gynecology and urology. The editors indicate that their purpose is, first, to illustrate well the principles of operative techniques in stages and, second, to have each procedure and subject described by a surgeon whose technical experience has been extensive for each particular subject. In essence, each contributor has written from his personal experience presenting the techniques of operative surgery which he prefers to employ. This arrangement the editors find does not always coincide with their views nor are the techniques advocated ones which they may choose to follow.

From the introduction it is implied that the reader audience anticipated is largely limited to surgeons skilled in surgery in general but perhaps not necessarily in a specific operation in particular. However, the surgical interne and junior resident may find material also of value here in that considerable space is devoted to such subjects as ligature and suture material, techniques of local anesthesia, positioning on the operating table, hemostasis, infusions and transfusions, diathermy, needle biopsy, the use of retractors, methods of dissection, drainage, preparation of the skin, techniques of suture, and radium needle insertion. Each of these subjects is described and profusely illustrated in Part I of this volume. Benefits, cautions, and hazards of these various topics are succinctly and clearly presented.

Certain minor inconsistencies naturally come to light in a volume of this type. For example, the percutaneous administration of local anesthesia containing adrenalin is advocated by the author of one section and condemned by that of another. In the discussion of the merits of intra-arterial transfusion, no mention is made that the same effect often attributed to the intra-arterial administration of blood can be obtained by the intravenous route when blood is administered under similar pressures and rates of flow.

The illustrations for the subjects on the excision of soft tissue wounds, primary, delayed primary, and secondary suture, and primary suture of severed vessel, nerve, and tendon are well illustrated by Lt. Col. R. S. Hunt, who also served as author of these same chapter headings.

Surgery of Trauma, which comprises Part II of this volume, is especially well done.

Part III of this volume is a presentation of general principles involved in operations in the abdominal cavity; specific surgical procedures are profusely and well illustrated pertaining to the stomach and the duodenum. Other aspects of abdominal surgery will appear in Volume II, which appears equally promising as the contributors compare favorably with those in Volume I.

Undoubtedly the outstanding feature of Volume I is its brevity and clarity of presentation. The techniques presented are not only informative but of interest to the surgeon

in the United States who perhaps may choose to employ different techniques than some of those advocated by many of the contributors. Nonetheless, this volume has much to recommend it, although admittedly a fair amount of technical detail is devoted to subjects with which the general surgeon already is thoroughly familiar, particularly those subjects in Part I. Minimum attention is devoted to the details of pre- and postoperative care, although that which is covered is not grossly deficient. This volume will have its greatest reader interest among surgical residents; it may not serve more than a reference to the experienced surgeon who may only choose to use this book as a means for comparison of the operations presented with those which he prefers. This latter use, however, is of more than passing interest to the surgeon concerned primarily with technical details.

Perhaps if any one practice stands out as different from that as currently employed in the United States, it is the extensive use of local anesthesia for major intra-abdominal operative procedures. This is a rather refreshing note in the face of increasingly complex general anesthesia so often characteristic of anesthesia at the present time in this country.

—J. Garrott Allen

Fractures, Dislocations and Sprains. By John A. Key and H. Earle Conwell. St. Louis, 1956, The C. V. Mosby Company. Pp. 1168. $20.00.

This is the complete treatise on the management of injuries to the bones and joints.

The book is divided into two parts. Part I deals with general principles including fracture equipment, the histology of repair of fractures, and basic principles of treatment. There is an excellent section on complications of fractures and methods of recognition and prevention.

Part II deals with diagnosis and treatment of specific injuries. These are well organized into regions with each section prefaced with a consideration of the surgical anatomy. Then specific injuries are discussed, dealing with age incidence, mode of injury, clinical and roentgen diagnosis, complications, and treatment. There is discussion of the management of nonunion and aseptic necrosis.

This book, as in its previous editions, satisfies a real need as a basic reference in the treatment of fractures, dislocations, and sprains. It is an outstanding and authoritative presentation of the subject, based upon a lifetime of clinical experience which is reflected in the critical judgment and wisdom of the authors. This is more than a text and will serve well the needs of the experienced orthopedic surgeon and will also provide a ready source of practical information for the student and resident. With Dr. Key's recent death this book serves as a living reminder of one of the outstanding leaders in the field of orthopedics.

—David W. Anderson

Tho Stress of Life. By Hans Selye. New York, 1956. McGraw-Hill Book Company, Inc. $5.95.

In this book, Dr. Selye writes primarily for the layman on the subject of what Medicine has learned about stress. It is a volume which has many facets; in one sense it is an autobiography, in another it is a philosophy of life, and still another it is an account of his enthusiasms and frustrations in conjunction with his studies on stress, but most important also, it is pleasant reading.

This volume is divided into 5 Books or sections dealing, respectively, with the Discovery of Stress, the Dissection of Stress, the Diseases of Adaptation, a Search for Unified Theory, and Implications and Applications. In each section the author presents very clearly his concepts and his interpretations of data relative to his concept of stress: the latter term he defines as the wear and tear of life, perhaps serving as a unified theory for the basis of disease. He attempts to delineate between the stressful response and the stressor—the insighting phenomenon. The roles of his alarm reaction, that of resistance, and the role of exhaustion are clearly discussed as he sees and interprets them in relation to his general adaptation syndrome. His thesis to the layman will be convincing but admittedly it is not always possible in this volume for the novice to delineate fact from theory and unbridled imagination.

This is an interesting exposé of Selye's ideas presented as a thesis. Despite the fact that many will disagree severely with many of his conclusions, it is this reviewer's impression that his volume will be of interest, largely as a science writer's insight to his problem. As such, the book should enjoy an extensive circulation, particularly among laity, many of those on the periphery of science, and probably also among some physicians and physiologists. Undoubtedly the author does not intend that this book should serve a more profound purpose.

—J. Garrott Allen

Calendar of Surgical Meetings

1957

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY. *Annual Meeting,* May 4, 6, and 7, 1957, The Palmer House, Chicago, Ill. Deadline for papers, Dec. 15, 1956. Secretary, H. T. Langston, M.D., 1919 West Taylor St., Chicago 12, Ill.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS. *Annual Meeting,* May 1, 2, and 3, 1957, The Homestead, Hot Springs, Va. Secretary, John A. Taylor, M.D., 2 East 54th Street, New York 22, N. Y.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA. *Annual Meeting,* Oct. 31, Nov. 1 and 2, 1957, The Homestead, Hot Springs, Va. Deadline for papers, Aug. 1, 1957. Secretary, James K. Stack, 700 N. Michigan Ave., Chicago 11, Ill.

AMERICAN COLLEGE OF SURGEONS. *Sectional Meetings,* 1957: Feb. 4-7, Hotels Jung and Roosevelt, New Orleans, La.; Feb. 28-March 2, The Olympic Hotel, Seattle, Wash.; March 18-20, The Sheraton-Park Hotel, Washington, D. C.; March 25-27, The Royal York, Toronto, Ontario. *Clinical Congress,* Oct. 14-18, Convention Hall, Atlantic City, N. J. Secretary of the College, Michael L. Mason, 154 E. Erie St., Chicago 11, Ill.

AMERICAN GYNECOLOGICAL SOCIETY. *Annual Meeting,* May 27, 28, and 29, 1957, The Homestead, Hot Springs, Va. Secretary, Andrew A. Marchetti, M.D., Georgetown University Hospital, Washington 7, D. C.

AMERICAN MEDICAL ASSOCIATION. *Annual Meeting,* June 3-7, 1957, Coliseum, New York, N. Y. Deadline for papers, Dec. 15, 1956. *Clinical Meeting,* Dec. 3-6, 1957, Auditorium, Philadelphia, Pa. Deadline for papers, July 15, 1957. Secretary, American Medical Association, George F. Lull, M.D.; Secretary, Council on Scientific Assembly, Thomas G. Hull, M.D.; address of both, 535 North Dearborn Street, Chicago 10, Ill.

AMERICAN SURGICAL ASSOCIATION. *Annual Meeting,* May 8, 9, and 10, 1957, The Palmer House, Chicago, Ill. Secretary, R. K. Gilchrist, M.D., 59 East Madison Street, Chicago 3, Ill.

AMERICAN UROLOGICAL ASSOCIATION. *Annual Meeting,* May 6-9, 1957, William Penn Hotel, Pittsburgh, Pa. Deadline for papers, Jan. 1, 1957. Secretary, Samuel L. Raines, M.D., 188 S. Bellevue Blvd., Memphis, Tenn.

THE CENTRAL SURGICAL ASSOCIATION. *Annual Meeting,* Feb. 21-23, 1957, The Drake Hotel, Chicago, Ill. Deadline for papers, Oct. 15, 1956. Secretary, Charles D. Branch, M.D., 102 North St., Peoria, Ill.

THE HARVEY CUSHING SOCIETY. *Annual Meeting,* April 25-27, 1957, Hotel Statler, Detroit, Mich. Secretary, David L. Reeves, M.D., 316 W. Junipero St., Santa Barbara, Calif.

NEW ENGLAND SURGICAL SOCIETY. *Annual Meeting,* Oct. 4 and 5, 1957, Mount Washington Hotel, Burton Woods, N. H. Deadline for papers, June 1, 1957. Secretary, Richard Warren, M.D., Peter Bent Brigham Hospital, 721 Huntington Avenue, Boston 15, Mass.

THE PACIFIC COAST SURGICAL ASSOCIATION. *Annual Meeting,* Feb. 4-6, 1957, El Mirador Hotel, Palm Springs, Calif. Secretary, Carleton Mathewson, Jr., M.D., Stanford University Hospital, San Francisco 15, Calif.

PAN-PACIFIC SURGICAL ASSOCIATION. *Annual Meeting,* Nov. 14-22, 1957, Honolulu, Hawaii. Director General, F. J. Pinkerton, M.D., Room 230, Young Building, Honolulu, Hawaii.

THE SOCIETY OF UNIVERSITY SURGEONS. *Annual Meeting,* Feb. 7-9, 1957. the Deshler-Hilton Hotel, Columbus, Ohio. Abstracts to be received by Dr. Ben Eiseman, Chairman, Committee on Publications, 4200 E. Ninth Ave., Denver 20, Colo., by Nov. 15, 1956. Secretary, James D. Hardy, M.D., Hospital of the University of Mississippi, Jackson, Miss.

THE SOCIETY FOR VASCULAR SURGERY. *Annual Meeting,* June 2, 1957, Hotel Biltmore, New York, N. Y. Secretary, Henry Swan, M.D., 4200 E. 9th Avenue, Denver, Colo.

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